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TRACKING PULSE OXIMETER FINDINGS BEFORE, DURING AND AFTER TITRATION OF MANDIBULAR ADVANCMENT DEVICES (MAD) FOR PATIENTS WITH MILD TO MODERATE OBSTRUCTIVE SLEEP APNEA (OSA)

by

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A thesis submitted to the Faculty of the
Orofacial Pain Graduate Program
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Uniformed Services University of the Health Sciences
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Master of Science
in Oral Biology

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Naval Postgraduate Dental School
Uniformed Services University of the Health Sciences
Bethesda, Maryland

CERTIFICATE OF APPROVAL

MASTER'S THESIS

This is to certify that the Master's thesis of

Jaime K. Lee

has been approved by the Examining Committee for the thesis requirement for the Master of Science degree in Oral Biology at the June 2015 graduation.

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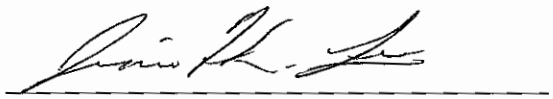

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ABSTRACT

TRACKING PULSE OXIMETER FINDINGS BEFORE, DURING AND AFTER TITRATION OF MANDIBULAR ADVANCMENT DEVICES (MAD) FOR PATIENTS WITH MILD TO MODERATE OBSTRUCTIVE SLEEP APNEA (OSA)

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INTRODUCTION:

The maximum tolerable jaw protrusive setting on a mandibular advancement device (MAD) for an obstructive sleep apnea (OSA) patient is believed to optimally open the airway and reduce apnea-hypopnea index (AHI) as measured by polysomnography (PSG). However, the objective data to support this contention are inconclusive. There may be a range of sub-maximal jaw protrusion settings that achieve the desired improvement in OSA symptoms. Analysis of nightly pulse oximetry (pulseox) data during home titration of a MAD may indicate when optimal protrusion is achieved.

OBJECTIVE:

Pulse oximeters can produce an oxygen desaturation index (ODI) that may be comparable to the AHI determined by PSG. The purpose of this study is to track ODI during: 1) the diagnostic PSG; 2) nightly titration of a MAD; and 3) the post-titration PSG when titration-derived mandibular protrusion is set on the MAD.

METHODS:

This pilot study will enroll 20 participants with mild to moderate OSA, treated by conventional 6-8 week MAD self-titration, with monitoring via nightly pulseox and daily diaries. Data collected will: compare ODI and AHI at the diagnostic PSG and at the post-titration PSG; correlate ODI with standardized sleep quality questionnaires; correlate

ODI with changes in mandibular protrusion and with patients' subjective daily sleep quality, comfort, and stress; and assess whether initial ODI or AHI at the diagnostic PSG correlates to compliance for wearing MAD.

RESULTS:

This study is in proposal stage due to numerous pulseox device networking obstacles, and thus no results have been obtained.

CONCLUSION:

No previous study has tracked real time, nightly ODI for correlations with AHI, subjective measures, and jaw protrusion. Pulse oximetry may be able to objectify titration of MADs while treating OSA to achieve optimal protrusion and reduce the need for expensive full night post-titration PSGs.

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LIST OF ABBREVIATIONS

AARC	Association for Respiratory Care
AASM	American Academy of Sleep Medicine
AHI	Apnea-hypopnea index
APAP	Automatically self-adjusted positive airway pressure
APPX	Appendix
BiPAP	Bi-level positive airway pressure
CNS	Central Nervous System
CO2	Carbon dioxide
CPAP	Continuous positive airway pressure
CPR	Cardiopulmonary resuscitation
CRADA	Cooperative research and development agreement
CT	Computer Tomography
ECG	Electrocardiogram
EEG	Electroencephalogram
EOG	Electro-oculogram
ESS	Epworth sleepiness scale
FOSQ	Functional outcomes of sleep questionnaire
ICSD	International Classification of Sleep Disorders
IRB	Institution Review Board
MAD	Mandibular advancement device
MRA	Mandibular repositioning appliances

MRI	Magnetic resonance imagery
NPDS	Naval Postgraduate Dental School
OA	Oral appliance
ODI	Oxygen desaturation index
OSA	Obstructive sleep apnea
OSAHS	Obstructive sleep apnea-hypopnea syndrome
PAP	Positive airway pressure
PI	Principal investigator
POB	Posterior open bite
PSG	Polysomnography
PSS	Perceived stress scale
PSQI	Pittsburgh sleep quality index
RERA	Respiratory effort-related arousals
RDI	Respiratory disturbance index
SaO2	Arterial oxygen saturation
SAHS	Sleep apnea-hypopnea syndrome
SDB	Sleep disordered breathing
SNS	Sympathetic nervous system
SpO2	Peripheral oxygen in the blood
TMD	Temporomandibular disorder
TMJ	Temporomandibular joint
UPPP	Uvulopalatopharyngoplasty
VAS	Visual analogue scale
WRNMMC	Walter Reed National Military Medical Center

CHAPTER I: INTRODUCTION

Sleep-disordered breathing (SDB) refers to a spectrum of disorders characterized by abnormal respiratory patterns, and specifically, pauses in breathing. These disorders span intermittent snoring to sleep apnea-hypopnea syndrome (SAHS) (Dieltjens et al., 2012). While snoring may not always have adverse physiological effects, SAHS is associated with daytime sleepiness and cognitive issues and increases the risk of developing health problems such as hypertension, arrhythmias, and diabetes, as well as stroke and premature death from cardiovascular disease (Ross et al., 1998; Young et al., 2009).

Sleep apnea was not defined as a medical problem until 1966 (Gastaut et al., 1966) and the only effective treatment to open the airway during that time frame was tracheotomy, reserved only for severe cases (Young et al., 2009). Continuous positive airway pressure (CPAP) delivered through a mask to open the airway became available in 1981 (Sullivan et al., 1981; Young et al., 2009) and oral appliances (OA) were introduced to advance the jaw and open the airway in the 1980s (Hoffstein, 2007).

Today, SDB is still an emerging area of medicine. Many questions have been addressed by the 1999 American Academy of Sleep Medicine (AASM) Task Force and the 2005 and 2014 editions of the International Classification of Sleep Disorders (ICSD). Definitions for conditions and codes for clinical practice have been established, and recommendations for diagnostic, treatment and research techniques have been presented

(AASM Task Force, 1999; AASM ICSD, 2005, 2014). Although advances have been made, uncertainty persists about the optimal way to treat OSA with MAD.

CHAPTER II: REVIEW OF THE LITERATURE

Types of Sleep Apnea

Three forms of sleep apnea are recognized: central, mixed and OSA, by far the most prevalent type of sleep apnea (Dempsey et al., 2010). Central and mixed sleep apneas involve dysfunction in the central nervous system (CNS) that results in inadequate or complete cessation of breathing effort during sleep. OSA, on the other hand, is due to recurrent episodes of complete or partial blockage of the airway despite normal CNS respiratory effort. These episodes reduce blood oxygen saturation (hypoxemia), increase carbon dioxide levels (hypercapnia), induce arousals from sleep and cause abnormal pauses in breathing that can last longer than ten seconds (AASM Task Force, 1999; Malhotra & White, 2002; AASM ICSD 2014).

Apnea is cessation of breathing attributed to *complete airway obstruction* during sleep. Hypopnea involves episodes of shallow breathing or a low respiratory rate that does not meet metabolic needs and is attributed to *partial airway blockage* (Dempsey et al., 2010). An obstructive apnea or hypopnea event, by definition, lasts at least 10 seconds and meets one of the two following features (AASM Task Force, 1999):

1. Substantial reduction in airflow (> 50%) relative to a baseline of the preceding two minutes.

2. Moderate reduction in airflow (< 50%) with blood oxygen desaturation (> 3%) relative to a baseline of the preceding two minutes or an electroencephalographic evidence of arousal.

Since apnea and hypopnea share similar pathophysiology, they are categorized under the same label, obstructive sleep apnea-hypopnea syndrome (OSAHS) (AASM Task Force, 1999). OSAHS is a subset of the more general SAHS, and although OSAHS is the most accurate acronym, many authors simply use OSA, which is employed in this proposal.

AHI

The severity of the OSA is measured by AHI which the AASM task force (1999) defined as the rate of obstructive apnea/hypopnea events per hour of sleep. PSG measures multiple physiological parameters during an overnight sleep study and is viewed as the ideal method for determining AHI. The AHI index, initially established by the 1999 AASM Task Force, was recently updated (AASM ICSD, 2014) and is listed below:

1. Mild 5 to 15 events per hour*
2. Moderate > 15 to 30 events per hour
3. Severe > 30 events per hour

*Mild OSA must also include one of the following:

- Sleepiness, unrestored sleep, fatigue or insomnia complaints

- Waking up with breath holding, gasping or choking
- Observed habitual snoring, breath interruption or both
- Diagnosis of hypertension, mood disorder, cognitive dysfunction, coronary artery disease, stroke, congestive heart failure, atrial fibrillation, or type 2 diabetes mellitus.

RDI

Respiratory Disturbance Index (RDI) is also used in sleep medicine but has had a varied definition (Epstein et al., 2009). Like AHI, RDI is an hourly average and uses the same numeric range as AHI to define mild, moderate and severe OSA. However, in addition to measuring apnea and hypopnea, RDI also includes less severe respiratory effort-related arousals (RERA). These events involve reduced airflow but do not meet oxygen desaturation criteria for hypopnea. RDI can be derived from PSG but it can also be assessed by portable monitors that do not differentiate whether or not the patient is sleeping. Since portable monitors collect data at night when the patient is not always asleep, these measures of RDI can underestimate OSA severity (Park et al., 2011). RDI measured from oximetry during PSG may slightly overestimate AHI, but it correlates closely with AHI for OSA patients (Vasquez et al., 2000). RDI closely correlates with AHI when the definition of hypopnea includes a reduction in thoracoabdominal movement for at least 10 seconds and either (*1*) a $\geq$ 4% reduction in SaO2 or (*2*) either a $\geq$ 4% decrease in SaO2 or an arousal. RDI does not correlate with AHI when only an

electroencephalographically based arousal counts are also included among hypopnea events (Tsai et al., 1999).

OSA Prevalence

Loud snoring, a possible precursor of OSA, afflicts 40% to 60% of all adults and is considered the most prevalent sleep disorder (Ohayon et al., 1997). Loud snoring, sleep arousals due to gasping for breath, and poor sleep quality are hallmark signs of OSA. OSA, often considered a mechanical issue, is implicated in the pathogenesis of a variety of other conditions, such as increased risk for cardiovascular disease, that are related to poor autonomic nervous system control (AASM Task Force, 1999; AASM Guidlelines 2nd Ed, 2005).

Airway obstruction is the most common anatomical finding associated with sleep disorders, and affects 2% of middle-aged women and 4-5% of middle-aged men in North America (Kapur et al., 1999; Young et al., 2002). OSA represents 85% of all sleep apnea cases, 80% of which go undiagnosed (Kapur et al., 1999). Fifteen years ago, untreated sleep apnea cost the U.S. society more than $3.4 billion annually due to medical costs (Kapur et al., 1999). Perhaps 15% of the U. S. population endures untreated sleep apnea (Young et al., 2009). Common consequences of undiagnosed OSA include excessive daytime sleepiness, impaired cognitive performance, and reduced quality of life. These symptoms may result in neuropsychological changes, such as decreased concentration, memory effects, and an elevated risk for motor vehicle accidents (Teng & Won, 2012).

Daytime sleepiness and fatigue can cause periods of inattention, decreased productivity and safety related hazards in the work place.

OSA induced effects are of concern to military service members. An epidemiologic study conservatively estimated the prevalence of mild OSA at 5% of males in the general population (Young et al., 2002). At this rate, 70,000 of the 1.4 million active duty military members (DMDC, 2013) may have OSA and possibly benefit from treatment. In addition, veterans are four times more likely to suffer from OSA than the general population (Teng & Won, 2012).

Dentistry, Oral Appliance and CPAP Therapy, Titration

The definitive diagnosis of OSA is not within the scope of dentistry. However, referral of patients diagnosed with OSA by a sleep physician to dentists trained in sleep disorder management is a viable cost-effective treatment option. Oral appliances offer a treatment option for OSA patients in addition to frequently cumbersome continuous positive airway pressure (CPAP) machines that generate air pressure to keep the airway open.

Mild to moderate OSA treated with oral appliances that advance the mandible forward to comfortably open the airway can improve OSA symptoms in up to 77% of patients (Dieltjens et al., 2012). Further, a recent cross-over design study compared one month use of an adjustable MAD to one month use of CPAP for patients with *moderate to severe OSA*. In terms of 24 hour mean ambulatory blood pressure, daytime sleepiness,

disease specific and general quality of life measures, MAD therapy was not inferior to CPAP treatment (Phillips et al., 2013). The findings of Phillips et al. (2013) challenge the premise that MAD therapy may not be appropriate for *moderate to severe OSA* (White & Shafazand, 2013). Fleury et al., 2004 also showed that over 80% OSA patients with a mean AHI of 46 who did not tolerate CPAP benefited from MAD therapy.

While CPAP is highly effective at opening the airway and reducing AHI for all levels of OSA severity, patient acceptance of CPAP is low. Consequently, compliance limits the clinical effectiveness of CPAP. MAD are sometimes as effective as CPAP in reducing the severity of OSA, and the self-reported compliance rate is higher for MAD since patients prefer the comfort of a MAD compared to CPAP (Dieltjens et al., 2012; Phillips et al., 2013). The compliance rate for MAD use is reported as a median of 77% of nights at one year for a treatment efficacy of 52% (Ferguson et al., 2006) while CPAP effectiveness due to compliance issues is 50% (Vanderveken & Hoekema, 2010; Grote et al.,2000).

The hourly/nightly difference in compliance for CPAP and MAD therapy was illustrated in a cross over study (Barnes et al., 2004). Mild to moderate OSA patients were initially randomized to 3 months of MAD or CPAP, and then crossed over to 3 months of the other therapy. Patients averaged CPAP use 4.2 $\pm$ 0.3 nights a week for 3.6 + 0.3 hours a night and MAD use 5.3 $\pm$ 0.3 nights per week for an average of 5.5 + 0.3 hours a night. MAD use as has been characteristic of such studies was collected by self-report. This was recently addressed in a 3 month prospective trial in which micro-sensors were embedded

in MAD (Vanderveken et al., 2013). In this trial participants reported MAD use by diary but were unaware that the temperature micro-sensors objectively reported MAD use as 6.6 + 1.3 hours per night for 82% of available nights. This objective measure did not statistically differ from use reported by diary. These objective findings combined with improvement in a variety of clinical parameters allowed calculation of the mean disease alleviation (MDA) effect for the MAD as 51.1% which compares favorably to CPAP efficacy (Grote et al., 2000). Higher treatment compliance rates for MAD result in improved prognosis for mild to moderate OSA (Dieltjens et al., 2012) and moderate to severe OSA that compare favorably with CPAP therapy outcomes (Phillips et al., 2013).

Optimal titration (setting protrusive position) of the MAD involves slowly advancing the mandible forward over time to a comfortable position that opens the airway and maximally reduces AHI. This is best accomplished over many nights/weeks in the patient's home environment. Currently, evaluation of MAD titration is assessed by subjective questionnaires, objective instrumentation such as PSG to measure AHI, or a combination of both. Ideally, an AHI assessment by PSG following a gradual MAD titration should be made. Unfortunately, that does not always happen. Also unfortunately, the jaw protrusion setting is often determined only during a single night sleep laboratory testing without the benefit of home titration. This approach does not allow the patient time to comfortably adapt to forward jaw positioning. At present, MAD titration to decrease the AHI is considered an inconsistent trial and error process (Dieltjens et al., 2012).

MAD titration performed over time in a patient's home sleeping environment may enhance compliance (Dieltjens et al., 2012). Home titration may reduce the cost and inconvenience of additional nights in a sleep laboratory for PSG. Currently, there is a need for a convenient, low cost objective titration protocol that maximizes the efficacy of the MAD to comfortably reduce AHI (Gauthier et al., 2012). Standardization of a comfortable MAD titration protocol that would minimize subjectivity while enhancing objective OSA treatment outcomes (reduced AHI) is a goal of the sleep medicine community.

CPAP therapy poses problems for deployed military personnel. CPAP machines are cumbersome, noisy, challenging to fit, hard to maintain, and require electricity to power the device. They can cause claustrophobia, breathing difficulty, airway dryness, congestion, and irritation (Massie et al.,1999). The austere environments to which military members with mild to moderate OSA may be assigned may interfere with adequate use and maintenance of CPAP. Such deployed military members may be ideal candidates for MAD therapy (Lettieri et al., 2011). MAD such as the TAP-3 Elite are small, lightweight, portable and free of electronics. Thus they do not require a power source and are deployment-friendly.

Pathophysiology

Airway anatomy, depressed upper airway muscle activity, and genetic predisposition are the main factors in the complex pathophysiology involved in airway collapse in OSA patients

(Deegan & McNicholas, 1995).

CT (computed tomography) and MRI (magnetic resonance imaging) have shown during wakefulness that OSA patients have reduced upper airway size compared to similar weight and age-matched controls. Patients have smaller retropalatal areas with fat deposits around the upper airway (Horner et al., 1989; Schwab et al., 1993). A 1997 study that compared 17 healthy patients to 40 OSA patients found smaller pharyngeal airways and increased airway collapsibility in OSA patients (Isono et al., 1997).

Maintaining pharyngeal airway patency for breathing, speech or swallowing involves the brain's motor control system. During inhalation while awake, reflexive activity by up to 20 pharyngeal dilator muscles combats the negative pharyngeal airway pressure developed as the diaphragm and the intercostal muscles contract. This muscle activity minimizes narrowing or collapse of the airway and maintains air flow (Malhotra & White, 2002).

In OSA patients, upper airway dilator muscles are more active during daytime inspiration to maintain the airway compared to healthy individuals whose airways are not anatomically compromised (Mezzanotte et al., 1992). Another study also showed during wakefulness that OSA patients compensated for greater negative pressure through increased dilatory muscle activity. This increased effort enabled OSA patients to achieve the same air flow rate (fill lungs with the same amount of air) as healthy subjects (Fogel et al., 2001).

During sleep neuro-muscular reflexes are absent or greatly reduced. Even in healthy people,

the ability of the pharyngeal dilator muscles to respond to negative pressure is inhibited during sleep (Dempsey et al., 2010), but the explanation for this nocturnal inhibition of dilator muscles is not clear. During sleep, reduced excitatory input to the hypoglossal neurons may suppress the ability of the upper airway dilator muscles to reflexively respond, as they do during waking hours, to negative pressure and other stimuli (Malhotra & White, 2002).

Individuals with compromised airway anatomy are more vulnerable to airway closure during sleep (Malhotra & White, 2002). In OSA patients, reduced reflexive dilatory muscle activity during sleep results in greater reduction of airway patency than occurs in healthy individuals (Dempsey, 2010). Sleep-induced restriction of air flow initiates only a weak reflexive response to increase dilator muscle activity, and in OSA patients the increases are generally insufficient to re-establish pharyngeal patency (Berry & Gleeson, 1997; Gleeson et al., 1990).

As apnea or hypopnea develops during sleep, carbon dioxide (CO2) levels in the blood rise. Sympathetic nervous system (SNS) activity, increased by carbon dioxide chemoreceptors, leads to a sleep arousal and re-activates the dilatory muscle reflexes (Berry & Gleeson, 1997; Dempsey et al., 2010). The arousal induced dilator muscle activity improves airflow and decreases CO2 in the blood. Lower CO2 calms the arousal response, and the pharyngeal dilatory muscles again relax (Deegan & McNicholas, 1995). As a result, OSA patients are aroused from sleep repeatedly throughout the night to clear the apnea-induced hypoxemia, then relax back into sleep and begin a new OSA cycle. If the apneas occur with sufficient frequency, the patient does not progress through a full sleep cycle during the night (AASM

Task Force, 1999). It is this sleep fragmentation that leads to daytime drowsiness, negative health outcomes and decreased quality of life (Vanden Brook, 2010).

OSA Risk Factors

The principle OSA risk factors include age, male sex and obesity (Eckert & Malhotra, 2008). Particular risk factors that increase the probability for the onset of OSA include: (1) neck circumference > 17 inches for men, > 16 inches for women; (2) body mass index (BMI) > 35; (3) a Modified Mallampati score of 3 or 4; (4) craniofacial variation; (5) nasal obstruction; (6) pharyngeal crowding; (7) male sex; (8) increasing age; (9) hypertension; and (10) sedative use (Epstein et al., 2009; Culpepper & Roth, 2009).

The Modified Mallampati score (1-4) is determined by assessing the visibility of structures in the oral cavity (Nuckton et al., 2006).

- Class 1: Full visibility of tonsils, uvula and soft palate
- Class 2: Visibility of hard and soft palate, upper portion of tonsils and uvula
- Class 3: Only the soft and hard palate and base of the uvula are visible
- Class 4: Only Hard Palate visible

Individuals with scores of 3 or 4 who have accompanying daytime symptoms should be evaluated for OSA.

Diagnosis and Measurement

The diagnosis of sleep apnea must be made by a sleep physician. The full night PSG study is considered the gold standard for sleep apnea diagnosis as it provides objective measures of neurological, chemical and physical parameters directly related to SDB (Dieltjens et al., 2012). An OSA is confirmed if a PSG, or similar data recording instrumentation, shows an AHI of five or more apnea/hypopnea events per hour of sleep and there is no neurological evidence of CNS dysfunction. If mild to moderate OSA is confirmed, the patient may be referred to a dentist for treatment using a MAD. Patients with more severe OSA who fail CPAP may also be referred to MAD therapy (Fleury et al., 2004; Phillips et al., 2103).

Four types of instrumentation assess physiological aspects of sleep apnea.

- Type 1: The full night PSG conducted by a sleep lab attendant in a formal sleep lab uses eight or more channels (7-12 leads) to record data. A PSG includes: electroencephalogram (EEG), electrocardiogram (ECG), electro-oculogram (EOG), electromyogram (EMG), nasal/oral airflow, chest/abdominal respiratory effort, AHI, blood oxygen saturation, ODI, respiratory disturbance index (RDI), and respiratory effort-related arousals (RERA) experienced per hour of sleep (AASM Task Force, 1999; Epstein et al., 2009).
- Type 2: Instrumentation gathers many of the same parameters as a PSG but does not use a sleep lab attendant. Portable Type 2 sleep monitoring devices require intensive training of patients, or assistance from well trained technicians and manual scoring of recordings by certified PSG technologists.

- Type 3: These monitoring devices record at least four parameters, including two pulmonary functions, heart rate, and blood oxygen saturation via pulse oximetry. While not as definitive as Type 1 or Type 2 instrumentation, Type 3 packages can be used in a home sleep environment and still give the sleep physician sufficient data on which to base a diagnosis (Collop et al., 2012; AASM ICSD, 2014).
- Type 4: These devices typically measure less than four parameters, but always include a pulse oximeter. Type 4 devices are inexpensive and easy to use at home. The simplest ones only measure pulse rate and blood oxygen saturation levels but do not provide sufficient objective data to positively diagnose OSA (Collop et al., 2012).

Pulse Oximetry: Objective Data to Monitor MAD Treatment?

Type 3 or 4 instruments with a pulse oximeter have high sampling frequency, high resolution and require little training. They detect fluctuations in oxygen saturation caused by episodes of apnea and hypopnea that can be analyzed by commercially available computer programs (Chung et al., 2012). In portable multichannel sleep screening devices that lack electroencephalographic or thoracic muscle activity monitoring capability, pulse oximetry is considered the most important parameter for identifying SDB (Netzer et al., 2001).

Pulse oximeters cannot definitively diagnose OSA since they cannot discern whether oxygen desaturation is due to OSA or some other cause, but they can be effective preliminary screening tools for SDB (Niijima et al., 2007; Chung et al., 2012). *Further,*

if a diagnosis of OSA using type 1, 2 or 3 instruments is confirmed by a sleep physician, an increased oxygen de-saturation index (ODI) derived from pulse oximetry data can be attributed to OSA (Collop et al., 2012).

The practice guidelines for pulse oximetry, published in 1991 by the American Association for Respiratory Care (AARC), recommend two uses for pulse oximetry:

1. As a warning signal for patients at risk for arterial desaturation.
2. For evaluating response to a therapeutic intervention or a diagnostic procedure.

This second recommended use is how the VirtuOx pulse oximeter is being used in this protocol to monitor home titration of a MAD. They are relatively inexpensive and easy to use. They can provide objective measurement of oxygen saturation levels that may enhance the ability of clinicians to determine what jaw protrusion setting on a MAD offers maximum airway function with minimal discomfort.

How a Pulse Oximeter Works

A pulse oximeter uses a non-invasive probe and a microprocessor to continuously measure the saturation level of peripheral oxygen in the blood (SpO2). It assesses the percentage of available hemoglobin saturated with oxygen. Although it is an indirect measurement of arterial oxygen saturation (SaO2), SpO2 closely correlates with actual oxygen saturation (Gries and Brooks, 1996). The probe has two light emitting diodes that emit red and infrared light (respective wavelengths of 660 nm and 940 nm) and photo

detectors that receive the light as it passes through a pulsatile tissue bed. The probe is typically worn on the finger, though a toe, ear lobe or the nose can be used. The microprocessor is worn on the wrist or lays in bed. It receives data from the photo detectors, detects the pulse of arterial flow and analyses the changes in light absorption in the tissue to yield SpO2 (Clark et al., 2006; Valdez-Lowe et al., 2009).

Blood highly saturated with oxygen allows more red light and less infrared light to pass through tissue to the photo detectors. As saturation decreases, less red light passes through the blood while the amount of infrared light that passes increases. The photo detectors measure the amount of light at each wavelength transmitted through the blood and sends this data to the microprocessor.

Awake, healthy individuals typically have SpO2 in the range of 97% to 99% when breathing room air (Schutz, 2001). Patients with normal hemoglobin who present with a SpO2 of 95% or greater are considered clinically acceptable (Clark, 2006). With age oxygen saturation rate tends to decrease. An average SpO2 below 90% indicates hypoxemia, a red flag to clinicians (Schutz, 2001). Only a weak relationship exists between average SpO2 during sleep and severity of OSA (Gries and Brooks, 1996; Tsai, et al., 1999).

A sudden SpO2 decrease of 3-4% over a period of less than 30 seconds may indicate an apnea event, but could also be an artifact of patient motion, or central nervous system or cardiac issues.

The average SpO2 calculated for the whole night blurs saturation variance and is of little utility in monitoring OSA activity (Tsai et al., 1999) and would not serve as a monitoring parameter in a MAD titration protocol.

Oxygen Desaturation Index (ODI)

ODI is the hourly average number of oxygen desaturation events defined as a decrease in SpO2 by 3-4% below the baseline level (average oxygen saturation during the preceding two minutes) that persist for greater than 10 seconds (Chung et al., 2012). ODI obtained from a pulse oximeter has a strong positive correlation with the AHI obtained from a sleep lab PSG (Chung et al., 2012). ODI slightly underestimated AHI by 1.6 events per hour (plus or minus 10) over the range of 5 to 30 events per hour but closely predicted AHI at 5, 15 or 30 events per hour which characterize mild, moderate and severe OSA as shown below (Chung et al., 2012).

- ODI greater than 5 was 87% accurate in predicting AHI of greater than 5
- ODI greater than 15 was 84% accurate in predicting AHI greater than 15
- ODI greater than 30 was 93% accurate in predicting AHI greater than 30

Chung et al. (2012) concluded that "ODI from a high-resolution nocturnal oximeter is a sensitive and specific tool to detect undiagnosed SDB in surgical patients." Their findings reinforced conclusions from earlier studies (Tsai et al., 1999; Magalang et al.,

2003; Vazquez et al., 2000) that ODI derived from a finger mounted pulse oximeter has excellent correlation with AHI derived from PSG in a sleep laboratory setting.

Limitations of Pulse Oximetry

Although high resolution pulse oximetry is a convenient and inexpensive way to screen for SDB, it has limitations. Because it only measures the oxygen saturation change and does not monitor nasal flow and respiratory effort, it is not able to distinguish OSA from central sleep apnea (Chung et al., 2012).

Pulse oximetry relies on pulsatile blood flow for its measurements and is vulnerable to the effects of poor peripheral arterial blood flow. Bodily movements, vasoconstriction and hypotension can cause artifacts through an interruption of the pulse signal. Since pulse oximeters do not always detect movement, artifacts due to motion would overestimate the number of de-saturations (Netzer et al., 2001).

Subjective Data and Pulse Oximetry

The value of pulse oximetry in SDB studies can be enhanced by combining it with simultaneous collection of subjective data. Using pulse oximetry data with a validated questionnaire like the ESS doubles specificity of oximetry as a screening tool for sleep apnea by cutting in half the number of misclassified cases (Nuber et al., 2000). This

study confirmed an early study that used a clinical sleepiness scoring system in conjunction with pulse oximetry data (Williams et al., 1991).

One study enrolled 68 patients with a high likelihood ($\geq$ 90%) of having moderate to severe OSA (AHI >15) based on ESS score, Sleep Apnea Clinical Score and overnight oximetry. They were randomly assigned to either PSG titration for CPAP or ambulatory titration using auto-CPAP and overnight oximetry. They were followed for 3 months and a post titration PSG was conducted. Initial PSG offered no advantage over subjective data and pulse oximetry for the diagnosis and treatment of patients with mild to moderate OSA, and the ambulatory approach appeared to enhance treatment compliance (Mulgrew et al. 2007).

Dentists can use the subjective questionnaires like the ESS and ask patients about sleep quality and snoring when assessing risk factors for OSA (Young et al., 2002). During an oral examination, dentists can evaluate for risk factors such as retrognathia (under developed jaw size), obesity and size of the upper airway using the modified Mallampati score. A one point increase in the modified Mallampati score increases the risk of OSA by a factor of 2.5 (Nuckton et al., 2006). Neck measurements greater than 17 inches in men indicates higher risk for OSA (Nuckton et al., 2006). If the ESS and the dental exam suggest significant sleep issues, the patient should be referred to a sleep physician for definitive tests.

The Walter Reed National Military Medical Center (WRNMMC) sleep laboratory uses two subjective questionnaires during diagnosis and assessment of treatment, the ESS and the

Functional Outcomes of Sleep Questionnaire (FOSQ). The Orofacial Pain Center also uses the ESS, the Pittsburg Sleep Quality Index (PSQI) and Perceived Stress Scale (PSS) as subjective questionnaires to assess diagnosis and treatment outcomes. Each of these instruments are available on the public domain for clinical and research use.

Methods of OSA Treatment

Sleep physicians have a range of treatment options for OSA patients. For mild OSA based on AHI, the first treatment of choice is patient education that reviews lifestyle changes and adjustments in sleeping habits (Malhotra &White, 2002). Lifestyle changes include weight loss, maintenance of nasal patency, avoidance of depressants such as alcohol close to bedtime, and a goal of seven to eight hours of sleep per night. For some patients with positional OSA, avoiding the supine position is effective (Malhotra & White, 2002).

CPAP has long been considered the gold standard medical therapy for OSA (Young et al., 1993; Qaseem et al., 2013) and is recommended for moderate and severe cases of OSA by the AASM (Kushida et al., 2005). Positive airway pressure (PAP) can improve the patency of an obstructed airway and CPAP is usually delivered through a face mask device (both nose and mouth or nasal only) to prevent airway collapse and maintain airway patency during sleep (Sullivan et al, 1981; AASM Task Force, 1999; Qaseem et al., 2013).

CPAP therapy improves sleep quality because positive pressure can be adjusted to significantly reduce apneas, hypopneas and snoring. It improves oxygen saturation during all

stages of sleep. Successful CPAP therapy improves the quality of life and decreases excessive sleepiness and depression while improving cognitive function and blood pressure (Bazzano et al., 2007; Qaseem et al., 2013).

Unfortunately, many patients do not tolerate CPAP because of claustrophobia, noise, nose bleeds, dermatitis and nasal bridge sores. In many cases, these effects are due to incorrect pressure settings or inadequate fit of the device on the face. Due to such discomforts only 60 to 80% of patients will use CPAP (Hsu & Lo, 2003). When the compliance rate is combined with CPAP efficacy CPAP effectiveness is as low as 50% (Grote et al., 2000). Such poor clinical adherence to CPAP supports the need to find other approaches to treat sleep apnea.

Other PAP therapies include bi-level positive airway pressure (BiPAP) and automatically self-adjusting positive airway pressure (APAP) devices. BiPAP mimics normal breathing more closely than CPAP. APAP devices detect the variability of airway resistance on a breath to breath basis, and vary the air pressure to provide the lowest and most comfortable positive pressure needed to keep the airway patent. These alternative PAP devices may be better tolerated than the CPAP (Culpepper & Roth, 2009).

For the more severe OSA cases, surgical procedures are treatment options. Surgery for OSA aims to relieve obstruction by increasing the size of the airway. Tonsillectomy and/or uvulopalatopharyngoplasty (UPPP) remove excess tissue to open the upper airway. However, positive results from these irreversible procedures have been inconsistent, ranging from 16% to 83% (Khan et al., 2009). A review, which noted that oral device treatment

lowered AHI more significantly than UPPP, did not provide evidence to support the use of surgery in patients with mild to moderate OSA (Sundaram et al., 2005).

With compliance for CPAP therapy difficult for many OSA patients, oral appliance therapy has emerged as a viable option (George, 2001; Hoekema et al., 2004; Hoffstein, 2007). Mandibular repositioning appliances, frequently referred to as a MAD, are the most common and effective oral appliances. A MAD is fitted to the maxillary and mandibular dentition, worn at night and can be variably adjusted to move the lower jaw forward and advance the base of the tongue. Such forward positioning increases pharyngeal airway space and reduces airway instability (Chan et al., 2007; Culpepper & Roth, 2009; Dieltjens et al., 2012). Greater mandibular protrusion is associated with increased MAD efficacy in reducing the AHI (Kato et al., 2000). The amount of mandibular protrusion achievable is limited by patient anatomy and tolerance.

A review on oral appliances, including MADs, suggested that these devices decrease snoring and increase average SpO2 level in "a significant number" of patients (Ferguson et al., 2006). The various studies in the review used differing definitions of success. Studies that defined success as achieving an AHI $\leq$5, reported only a 42% level of successful treatment. Other studies used an AHI $\leq$ 10 as the definition of success and the average success rate for these was 52%. Still others accepted a 50% reduction in AHI compared to the diagnostic PSG as a goal, and 65% of these patients achieved success.

One study looked at treatment success rate based on OSA severity defined by baseline AHI.

Between 14% and 61% of patients with severe OSA (AHI>30) achieved "success" (variably defined) while 57% to 81% of patients with mild to moderate OSA (AHI≤30) achieved "success" (Ferguson et al., 2006). The review also found that 77% patients were still using their devices after one year. This level of patient compliance is 27% higher than the CPAP compliance rate of 50% (Grote et al., 2000).

MAD therapy has emerged as a conservative, non-invasive treatment option for patients with mild to moderate OSA (Cistulli et al., 2004; Chan & Cistulli, 2009; Hoffstein, 2007). Compared with CPAP, MAD therapy has a higher self-reported adherence and patient preference rate due to its ease of use (Chan et al., 2007; Ferguson et al., 2006; Phillips et al., 2013). In 2011, it was shown that there is no clinically relevant difference between MAD and nasal CPAP in the treatment of *mild to moderate* OSA when both treatment modalities are titrated objectively (Aarab et al., 2011). And in 2013, MAD therapy was shown not to be inferior to CPAP in the treatment of *moderate to severe* OSA (Phillips et al., 2013). Although perhaps less efficacious than CPAP for improving the PSG-verified AHI scores for OSA, patients prefer MAD and use it more often than CPAP.

Oral Appliance Design and Mechanism of Action

A variety of MADs with different designs that advance the mandible and bring the tongue and soft tissue forward to increase airway space are commercially available for OSA treatment (Aherns et al., 2011). MAD design has evolved from the mono-bloc devices in which the upper and lower parts were rigidly fixed together. These provided only one fixed

setting for jaw advancement, and by fixing mandibular position, were more likely to induce temporomandibular joint (TMJ) pain (Tanoue et al., 2009). They are being replaced by the current duo-bloc MAD which enable titration (adjustment) of the mandibular protrusion.

Before initiating MAD titration, the appliance is set at a specific degree of jaw protrusion when it is first inserted for wear during sleep. An advancement mechanism enables a patient to self-adjust the appliance before going to sleep. This allows a patient to gradually protrude (or retrude) the mandible, based on symptoms, until a protrusive position with a positive OSA effect is achieved. The titration adjustments may be made at intervals ranging from a few hours by a sleep lab technician during a PSG study to once every few days during a home-use protocol prior to a second PSG study (Aarab et al., 2011).

Ideal treatment for OSA is provided by a multidisciplinary team that includes a sleep physician and a dental practitioner with expertise in the management of sleep disorders. The specific roles of physicians and dentists in the treatment of snoring and OSA with MAD have been defined by AASM task forces. Before treating, an objective assessment by a sleep physician is required. Based on the diagnosis, the physician decides if the patient is a good candidate for a MAD and makes a referral to the dentist (Kushida et al., 2005). The referral to the dentist should include a copy of the PSG findings, the ESS score, and pertinent medical information (Ferguson et al., 2006).

Upon referral, the dentist assesses the suitability of the patient's dentition for customized MAD treatment (Chan et al., 2007). This assessment includes a complete dental/medical

history and examination of extra- and intra-oral tissues. Soft tissue anatomy, periodontal status, dental caries, the TMJ, muscles of mastication and nocturnal bruxism are assessed. Restorative dental treatment must be completed before the fabrication of the MAD since new restorations can interfere with the fit of a previously made MAD. Patients must have a minimum of six healthy, non-mobile teeth per arch and at least one posterior tooth per quadrant. They must be able to protrude their lower jaw at least 6 millimeters for the procedure to be effective (Ferguson et al., 2006; Campbell et al., 2009).

If the patient is a suitable candidate, the MAD is fabricated in accordance with the manufacturer's instructions and delivered to the patient. The patient is given instruction (including a booklet) on its care and how to titrate or adjust jaw position. A suggested starting point for the MAD is between 50-75% of the patient's maximum mandibular protrusion, which may be reduced if initially not tolerated (Ferguson et al., 2006).

Clinicians should select FDA approved MADs which can be found at the web site: http://www.ihatecpap.com/oral_appliance.html.

Side Effects of MAD Therapy

Mild and transient side effects are common with initial use of a MAD and generally decrease after one week of use (Bailey, 2005; Ferguson et al., 1997). Transient effects on salivation, gingival pain, tooth pain, interference with oral breathing (if appliance is too bulky) and morning-after occlusal (bite) changes are reported in 6%-86% of patients (Ferguson et al.,

2006; Pancer et al., 1999). Other common side effects include myalgia and TMJ sounds. These symptoms, observed in 0%-75% of patients, also are usually temporary and resolve within several days to several weeks with regular appliance use and adjustment (Ferguson et al., 1997; Ferguson et al., 2006; Mehta et al., 2001).

Transient signs and symptoms for temporal mandibular disorder (TMD) occurred in a small number of patients who were pain-free before starting MAD treatment for OSA (Perez et al., 2013). TMD symptoms decreased over time during MAD titration. At the third follow-up visit, TMD symptoms affected 19.4 % of patients but only 8.2% of patients by the final visit. Patients with pre-existing TMD signs and symptoms did not experience an increase of symptoms with MAD use (Perez et al., 2013).

Long term use of a MAD can cause occlusal changes (Almeida et al., 2006). One of the most prevalent long term side effects due to MAD use is posterior open bite (POB). An average incidence of POB occurred in 17.9 % of patients who used a MAD more than one year. However, only 28.6 % of the 17.9% of patients with POB, observed by the dentist, were aware of any changes to their bite. This means that only 5.1% of all patients receiving MAD therapy for a year were aware of any bite changes. Morning jaw exercises that help relax the jaw muscles quickly counteract open bite changes (Perez et al., 2013).

Titration Methods

Titration refers to adjustment of therapy and evaluation of clinical parameters during titration

can assess OSA treatment efficacy. For example, CPAP pressure can be varied while the AHI is monitored (Epstein et al., 2009), or a MAD can be adjusted to change mandibular protrusion while the ODI or the ESS score is monitored (Dieltjens et al., 2012).

CPAP-PSG

A full-night PSG is recommended for the diagnosis of a SDB problem, followed by additional PSG studies to titrate CPAP and verify its effectiveness. Usually the sleep lab technician can adjust positive air pressure during CPAP titration in response to AHI changes without waking the patient (Epstein et al., 2009). However, to save costs, a split-night study (an initial diagnostic PSG for a few hours, followed by CPAP titration on the same night) may give satisfactory results (Kushida et al., 2005).

MAD-PSG

Initial MAD designs used the mono-bloc construction that did not permit titration. Clinicians had just one chance to determine a protrusion setting that attempted to maximally reduce AHI without causing adverse symptoms. Today, fortunately, numerous FDA approved adjustable MADs make titration of jaw protrusion feasible. A review summarized numerous studies in which MADs were titrated to *optimal mandibular protrusion* during a single night PSG study before the patient used the MAD at home (Dieltjens et al., 2012). In most cases, the patients had to be awakened to adjust their MADs (Almeida et al., 2009; Kuna et al., 2006). Some labs used *experimental* devices which allowed sleep lab technicians to remotely titrate the MAD and minimize waking the patient (Dort et al., 2006; Tsai et al., 2004; Petelle et al., 2002). However, attempting optimal jaw protrusion in a single night in a sleep lab does

not allow the jaw muscles time to adapt to a significantly increased jaw protrusion position.

In the non-experimental clinical setting, the sleep lab technician periodically wakes the patient to adjust protrusive setting during a single night, sleep lab MAD titration protocol. Single night titration interferes with the patient's already compromised normal sleep cycle and can alter the ratio of the various stages of sleep. Since the severity of sleep apnea changes during the various stages of sleep, including REM sleep, the results of the MAD titration by a technician in a sleep lab can bias jaw protrusion settings (Almeida et al., 2009).

MAD-Home

The disruptive effects during the PSG lab titration can be reduced by lower cost home titration of the MAD. At home before sleep, the patients use subjective sleep quality measures like the ESS and degree of jaw comfort to judge how to adjust protrusion to open the airway and gain sleep quality benefit.

Home evaluations may also include objective measures. Portable Type 2 instruments are available and collect nearly all the measures of a PSG, but they are expensive. Portable Type 3 instruments are less expensive but not simple. They typically have four channels of recorded data; pulse oximetry, air flow from which an AHI is derived, snoring by sound, and head movement. These parameters have been shown to be comparable in diagnostic ability to PSG (Dieltjens et al., 2012; Westbrook, 2007).

A Type 4 pulse oximeter can also be used to monitor MAD titration in the home. Pulse

oximetry data can be used to derive ODI which, as stated earlier, is strongly correlated with the AHI and could serve as a monitoring parameter for MAD titration at home (Chung et al., 2012). However, other than one study (Fleury et al., 2004), little data exist in the literature on the use of a pulse oximeter to provide objective data for MAD titration. Fleury's study enrolled 44 OSA patients (mean AHI of 46 at baseline PSG) who had been intolerant of CPAP. ESS, snoring, jaw comfort and ODI readings guided MAD titration. Patients advanced their jaw at a rate of 1 mm each week, had weekly office visits and a post titration PSG. The number of jaw advancements patients made was compared to subjective and objective measures. Clinically, 28 patients (63.6%) improved with complete symptom resolution and AHI (5 ± 3). Limited OSA improvement was gained by 8 patients (18.2%) and 8 patients (4 dropped out) were not helped. Some patients (25%) continued to make jaw advancements because ODI >10 even though OSA symptoms had resolved. Additional jaw advancements were made by 20% of patients because OSA symptoms persisted despite ODI reduced to 6 ± 2 (Fleury et al., 2004).

Protocols that only rely on subjective data such as ESS scores, self-reported awakenings, and the snoring scores from bed partners are inaccurate indicators of the optimum protrusion position in MAD titration (Almeida et al., 2009; Antic et al., 2009). However, objective and subjective evaluations of MAD titration do not always reach optimal therapeutic endpoints (Levendowski et al., 2007; Fleury et al., 2004). Some patients may subjectively over-titrate based on the assumption that further advancement of the appliance is better. Others may under-titrate based on perceived improvement in subjective sleepiness outcomes, regardless of their objectively measured ODI levels (Almeida et al., 2009; Fleury et al., 2004).

Confounding Factors When Interpreting Results of MAD Titration

- **Sleep disturbances due to the sleep lab environment**

The sleep lab environment differs from a subject's home sleep environment and may disturb ongoing sleep patterns and influence the parameters measured by PSG. Some sleep lab effects can be recognized by an experienced sleep physician, but other effects may not be detected. For example, sleep position can affect the severity of OSA parameters. PSG instrumentation such as nasal air flow monitors and electrodes may influence the patient to use sleep positions that differ from the home environment. Such changes can introduce bias into the titration data and result in a sub-optimal jaw protrusion (Marklund et al., 1998; Rodway & Sanders, 2003).

- **Intolerance to "sudden" mandibular protrusions during a single night PSG**

If the MAD is not titrated prior to a single night PSG sleep study, the patient will be aroused multiple times when sleep lab technician adjusts protrusion settings on the MAD. A protrusion setting that attains a target AHI may be achieved during the PSG, but subsequent jaw discomfort may persist and inhibit MAD use because the advancement was performed in a matter of hours while sleep was frequently disturbed (Dort et al., 2006; Petelle et al., 2002). This possibility of a painful, less than optimal jaw protrusion can be minimized by slow titration over days or weeks in a home sleep setting. As opposed to the "sudden" protrusive

setting established in a sleep lab, home titration allows patients to comfortably accommodate to slowly advancing jaw protrusion.

- **Threshold standards**

Establishment of a valid protocol for MAD titration is confounded because the literature does not support a consensus for the clinically ideal AHI or ODI (Dieltjens et al., 2012). The literature shows many "target" levels for AHI ranging from 5 to as high as 20 events per hour, and discusses different levels for oxygen de-saturation as indications for clinical improvement (Almeida et al., 2009; Cistulli et al., 2004; Ferguson et al., 2006). Some investigators use 3% desaturation below the average level in the preceding two or three minutes. Others use 4 % in an attempt to achieve a higher specificity for detecting sleep apneas. With either setting, an oximeter can miss some respiratory events that are detectable by more robust instrumentation, such as hypopneas with less than 50% airflow reduction and a corresponding mild blood desaturation that is than 3% (Westbrook et al., 2005).

- **Different MAD Devices**

Design variations between different MADs could impact comfort and ease of self-adjustment and be confounding factors for titration efficacy (Ahrens et al., 2011; Fleetham & Almeida, 2010; Vanderveken & Hoekema, 2008). But no studies have been published that examine whether or not different MAD design features influence titration protocol outcomes (Dieltjens et al., 2012).

MADs take up space in the mouth, but the literature is inconclusive as to whether or not differences in vertical jaw opening affect the treatment of sleep apnea. All MADs have material thickness and placing them in the mouth could exceed in some patients their comfortable inter-occlusal distance or space in between the teeth when jaw muscles are relaxed (Ahrens et al., 2011; Nikolopoulou, et al., 2011; Pitsis et al., 2002; Rose et al., 2002). Pitsis et al., 2002 did not find a correlation between variable vertical jaw opening and MAD efficacy and simply recommended using an appliance that is comfortable.

- **Collection of ODI data to guide titration**

How does the clinician obtain real time ODI and subjective data to help decide when sufficient protrusion of the mandible has been reached? Fleury et al., 2004 were not explicit in how ODI readings were obtained and used by the patient or the clinician. Technology will now allow patients to wear a pulse oximeter and the data will be uploaded directly to a secure cloud account that clinicians can monitor on a nightly basis.

The guidelines of the Canadian Thoracic Society and the American Academy of Sleep Medicine recommend oral appliances to open the airway as a first-line therapy option for patients with mild to moderate OSA, or primary snoring (without apnea). Appliances must be custom adjusted to each patient to achieve maximum benefit. However, a standard titration protocol for appliance adjustment does not exist. There is a lack of

data, guidelines, or established protocols to guide dentists in the titration of oral appliances for the treatment of OSA (Gauthier et al., 2012).

A home MAD titration protocol that continuously collects objective and subjective data on patient response may help determine optimal titration of the MAD. Conventional subjective data for jaw pain and quality of life coupled with objective data collected using a low-cost portable monitor could be shared between the dentist and the sleep physician and enhance OSA care with oral appliances. However, since data for monitoring MAD titration efficacy with a portable device have yet to be verified, the Canadian Sleep Dental Association recommends that a follow-up assessment by a sleep clinic confirm that MAD treatment success has been achieved (Gauthier et al., 2012).

Currently, MAD titration for optimum efficacy is performed on a case by case basis. MAD manufacturers give only "rules of thumb" or trial and error directions for titrating MADs. Dentists who deliver MADs and provide adjustment appointments must rely on the sleep laboratory for a follow up PSG to establish the patient's AHI response to the titration effort. This approach may cause repeated visits to sleep labs for PSG and increases expense and inconvenience to patients.

Subjective data do not always give an optimum titration setting for a MAD. Often, at the follow-up PSG, a different protrusion setting can further lower AHI, but this new setting may not be optimum. First, the patient is not in the home environment and secondly, the patient is woken multiple times to make titration adjustments. As discussed earlier, a combination of

subjective questionnaires and objective data such as ODI in the home setting, which does not require waking up, may achieve nearly optimum appliance setting. This approach may prove to be the most clinically effective and cost-effective method for the treating dentist and attending sleep physician to establish and maintain the optimum adjustment of a MAD (Baily, 2011).

Titration of a MAD using a portable pulse oximeter to monitor treatment response for patients diagnosed with OSA may yield predictable improvement of AHI. Low cost portable pulse oximeters detect disturbances in blood oxygen saturation and can be used to compute ODI that is proportional to AHI. An up or down trend in ODI is equivalent to an up or down trend in AHI (Collop et al., 2012). Confirmation of close correlation between AHI and ODI may reduce the need for a final follow up PSG sessions following home titrations (Chung et al., 2012). To date, only one study has directly compared MAD titration using subjective measures only (pain and quality of life) to both subjective and objective measures using a pulse oximeter (Fleury et al., 2004).

These data may show that:

- A simple Type 4 instrument, such as a pulse oximeter from VirtuOx, Inc, may provide ODI readings that closely correlate with AHI determined at diagnosis and post titration assessment by PSG.
- Nightly ODI data may show when optimal titration is achieved, and how subjective factors in the home environment influence titration
- The sleep physician may deem that return to the sleep laboratory for post titration PSG

may not always be needed.

CHAPTER III: MATERIALS AND METHODS

This proposed pilot study will directly compare ODI to AHI during the initial diagnostic PSG for OSA diagnosis and at the post titration PSG to assess titration effect. It will also use pulse oximetry on a nightly basis over a multiple week titration protocol to plot ODI to MAD advancement and measures of pain, stress and quality of sleep. Collecting these parameters in this manner has not been done before. Such data will closely assess the response sensitivity of a patient to MAD titration, and enable an understanding of how multiple subjective parameters and ODI interplay to determine when the optimum MAD protrusion may be achieved.

The purpose of this study is to collect nightly real time ODI to assess whether optimum jaw protrusion for treatment of OSA can be determined using pulse oximetry.

There are four specific aims that when achieved should establish a justification to commit considerable resources to a statistically significant clinical trial. These aims are:

1. Compare ODI and AHI at the diagnostic PSG and at the post MAD titration PSG.
2. Correlate ODI with ESS, FOSQ, PSQI and PSS before and following titration.
3. Correlate ODI with changes in mandibular protrusion during titration and with:
    a. daily subjective sleep quality based on Visual analog scale (VAS)
    b. patient daily comfort based on VAS

c. patient daily stress based on VAS

4. Assess whether initial ODI or AHI at the diagnostic PSG relate to compliance for wearing MAD.

This study proposes to pursue the stated objectives using volunteer subjects recruited from the WRNMMC sleep laboratory. Patients are regularly scheduled for a diagnostic PSG in the Sleep Laboratory for a baseline AHI. As part of these appointments, they also complete the ESS and FOSQ. During the course of this study, patients will be informed by a short note that the staff would like to collect, with permission, a concurrent baseline ODI using a portable VirtuOx, Inc pulse oximeter (specific aim #1). This comparison of AHI and ODI is being performed because the use of portable pulse oximeters may become standard of practice in the future. This comparison of baseline AHI and ODI will not require the use of personal identifiers. The short note will also inform patients that if their sleep study diagnosis is mild to moderate OSA, they may be offered the opportunity to participate in a study where titration of a MAD for their OSA will be monitored by the VirtuOx, Inc pulse oximeter.

Patients who reply to their sleep physician that they are interested in participating in the study will be scheduled for an appointment with investigators at the Naval Postgraduate Dental School (NPDS) Orofacial Pain Clinic. At that appointment the investigator emphasizes that participation in the study is completely voluntary, and then provides a thorough explanation of the study and an evaluation to determine if they are eligible. Interested patients will be given as much time as needed to read the consent and HIPAA

documents. The investigator will verbally review the contents of the informed consent document and answer all questions and clarify that participation is voluntary. If not interested in participation or the patient does not meet inclusion/exclusion criteria, the investigator assures the patient that they still will receive care for their mild to moderate OSA as per the WRNMMC Sleep Disorders Clinic's standard practice. It will also be reinforced that the patient can exit the study at any time after consent is obtained and still receive standard care treatment of OSA.

Twenty Tricare eligible military health care beneficiary patients of the WRNMMC who meet inclusion/exclusion criteria will be consented. These subjects will complete the PSQI, ESS, PSS and FOSQ both before and after MAD titration (specific aim #2). They will not be blinded to their MAD treatment as use of the MAD is part of the study disclosure. They will complete VAS on sleep quality, pain, and stress in a daily diary and record the advancement of their jaw protrusive settings on a log sheet (specific aim #3). They will be blinded to the ODI data collected at night by wearing the VirtuOx, Inc pulse oximeter. This data will be uploaded automatically in real time to the internet cloud.

Completion of the home titration will be based on the subjective data approach used by dentists; advance the mandible as far as possible to improve sleep quality and not cause jaw pain. At the end of the home titration the investigators will compare ODI data, jaw protrusion settings and subjective data (specific aim #2); and compare the ODI to the AHI recorded during the diagnostic and post titration PSG. During the post titration PSG

the sleep technician will not adjust the MAD since the goal is to see if home titration and ODI will approximate post titration AHI (specific aim #1). Confounding variables including patient pre-conceptions, design features of the appliance, and medical co-morbidities will be addressed by inclusion and exclusion criteria and patient compliance.

The data collected in the daily logs will show if and when the subject actually uses the MAD. Non-compliance could occur for a number of reasons and predicting a compliance rate is not possible at this time. Correlation of compliance rate with the initial diagnostic session ODI will be performed to see if this parameter has any predictive value for compliance rate (specific aim #4).

Inclusion and Exclusion Criteria

In order to minimize variability of study results due to co-morbid factors, each candidate for the study is screened for compliance with the study's inclusion and exclusion criteria.

a. Inclusion Criteria

1. Diagnosis of mild or moderate obstructive sleep apnea ($AHI \geq 5 \leq 30$)
2. Tricare eligible military health care beneficiary
3. Age 18 or older
4. Available to participate in the study for six months
5. Agree to participate and complete patient form/diary

6. Have 6 or more healthy, non-mobile teeth per arch, and at least 1 posterior tooth per quadrant
7. Able to protrude the lower jaw forward $\geq$ 5 mm
8. Do not need any restorative, periodontal, or root canal dental treatment
9. Do not have evidence of intraoral soft tissue and bone pathology

b. Exclusion Criteria

1. No diagnosis of mild to moderate OSA
2. Under 18 years of age
3. $\leq$ 6 healthy teeth per arch
4. A quadrant without posterior teeth
5. Restricted jaw opening $\leq$ 25 mm
6. TMD symptoms that prevent MAD wear
7. Caries, periodontal disease, oral pathology
8. Previous upper airway intervention for OSA:

    -CPAP

    -MAD

    -Surgery
9. Diagnosis of Periodic Limb Movement (restless leg syndrome)
10. Use of nighttime supplemental oxygen therapy (pulmonary or cardiac issues that may interfere with blood oxygen saturation measurements)
11. Cannot tolerate 50% mandibular advancement

12. Maximum mandibular protrusion $\geq$ 14 mm

Note that prior to patient consent, each appointment with the WRNMMC Sleep Center is the same sequence that non-study participants follow. The only difference is the addition of the VirtuOx pulse oximeter in the initial sleep study. Based on the results of this study use of the VirtuOx at WRNMMC may become part of the normal clinical sequence.

At the Orofacial Pain Center, current patients being treated for OSA with a MAD have the same four-appointment sequence as will be used in this study. The difference is that the consent process for research occurs in the first appointment as well as instruction in the use of a pulse oximeter. The self-titration process is identical, other than asking participants to keep the daily diary. Patients with long maximum protrusions may have an extra interim appointment to add an extra hook mechanism to accommodate titration towards their maximum protrusion. This is a normal part of clinical care.

OSA Treatment Protocol as Modified for this Study

Pre-enrollment appointments

- Diagnostic PSG at the WRNMMC sleep laboratory
    - All patients will receive a one page note disclosing that the VirtuOx pulse oximeter is being used and that patients with mild to moderate OSA may be offered a chance to participate in a study.

- Appointment with sleep medicine physician to discuss PSG findings and treatment
    - Patients with mild to moderate OSA may be offered MAD study participation by their sleep doctor. If interested they are given an appointment with the Orofacial Pain Center for an evaluation by an investigator.
    - If not interested, they follow the WRNMMC OSA standard care.

1st appointment at Orofacial Pain Center for evaluation and possibly consent

- OSA Dental Sleep Evaluation (See APPX A); standard procedure for sleep apnea patients at the Center
    - The investigator reviews inclusion/exclusion criteria as part of the dental sleep evaluation.
    - Patients who qualify will be given the opportunity to provide consent.
    - Consent may be obtained.
- Patients are given the informed consent/ HIPAA document and the investigator reviews all aspects of the consent.
    - Patients not interested in study participation are referred back to the WRNMMC Sleep Disorders Clinic for OSA care.
- Patients who provide consent will have:
    - ESS, PSQI and PSS administered.
        - standard procedures in the Center for treatment.
    - Maximum incisal opening and jaw protrusion measured.
    - Alginate impressions made of the maxillary and mandibular jaws.

- Bite registration fabricated chair side using TAP-3 bite registration appliance (Pro Gauge)(See APPX P). The bite registration will be fabricated with polyvinylsiloxane or Blue Moose dental impression material.
- A 0 to 10 VAS for sleep quality, jaw pain, and stress administered for the baseline.
- Impressions and bite registration sent to NPDS lab for fabrication of TAP-3 Elite oral appliance (See APPX P).

Patients will be informed that the oral appliance, TAP-3 Elite, used in the study is the same appliance that is normally used to treat mild to moderate OSA patients at WRNMMC. The patients will be shown an example of the TAP-3 Elite and how it mechanically operates.

2nd appointment - MAD delivery (lab needs 30 days to fabricate the TAP-3 Elite)

- Deliver TAP-3 Elite with verbal and written instructions (See APPX J).
  - How to place the TAP-3 Elite intra-orally and how to hook the maxillary piece into the mandibular piece will be demonstrated.
  - Self-titration of the TAP-3 Elite will be reviewed including how to self-reduce the protrusive length if the patient experiences intolerable symptoms at a new protrusive length.
  - To reduce the probability of intolerable symptoms, all participants will start titration at 60% of their maximum protrusive length and stay at this setting for one week.

- The exception will be if a participant accidently unhooks their TAP-3 elite repeatedly at 60% protrusive length. In this case, the appliance will be advanced until the subject can no longer unintentionally unhook the appliance. This will be their starting length.

- The VirtuOx pulse oximeter, with oral and written training in its use (including wireless uploading of data) at night, is delivered. The device will be used until completion of the study and then it is returned.
- ESS, PSS and PSQI are administered.
- The Daily Log for subjective measures of jaw pain, sleep quality and stress is provided with instructions on how to fill out the daily 0 to 10 VAS (See AAPX K).
- Participants are to call investigator if they have any concerns or discomfort and are appointed for a one week follow-up session.

3rd appointment (one week later)

- Daytime sleepiness is assessed by having participant complete the ESS.
- TAP-3 Elite is examined and any adjustments for fit and comfort made.
- Review maintenance of Daily Log with patient.
- Titration is again reviewed, with patients instructed to advance the jaw 0.25 mm every other night as long as there is no discomfort.
    - If there is discomfort they can keep it at the current protrusion setting or decrease the setting by 0.25 mm.
    - How to fill out titration log is reviewed.

- Review use of the VirtuOx pulse oximeter.
- Check for completion of data logs from VirtuOx, Inc (See APPX L).
- Give reminder to call if there are any concerns.
- Inform patient to call for follow-up appointment when maximum protrusion or intolerance reached.

The TAP-3 Elite MAD has a maximum adjustment range of 5 millimeters with no modifications. There are, however, three different interchangeable parts (hooks) that advance the starting point in 5 millimeter steps (See APPX P). Thus, for patients who require more than 5 millimeters of total titration length, an interim visit between the standard 3rd and 4th appointments may be needed to change out the advancement hook for one of a different length.

4th appointment (four to eight weeks later) at Orofacial Pain Center

Titration continues until either the maximum advancement measured in appointment 1 is reached or the discomfort of the advanced mandible becomes intolerable. The time needed for the titration to reach this point is variable but is estimated to not exceed eight weeks. When the participant comes in for the 4th appointment:

- The titration is considered completed.
- The optimal protrusion level to maximally reduce AHI is considered established based on the subjective measures of sleep quality and jaw comfort.
- The participant is administered the ESS, PSQI and PSS.

- The daily log and titration logs are collected (See APPX M).
- The TAP-3 Elite is set based on subjective data.
- The participant wears the TAP-3 Elite at this protrusion setting and continues using the pulse oximeter for one more week.
- The patient is scheduled for a post-titration evaluation in the sleep lab after this one-week settling period.
- Participants will be instructed to continue to complete the daily VAS log and continue using the pulse oximeter.

5th appointment - Post titration PSG at Sleep Disorders Clinic Sleep Lab (one week after completion of titration)

- The participant completes post titration ESS and FOSQ.
- The participant, while wearing the TAP-3 Elite and the VirtuOx pulse oximeter, undergoes another standard full night PSG to assess AHI achieved by the home titration (This is same titration appointment that non-study participants receive).
- The participant returns the VirtuOx pulse oximeter to the sleep lab but keeps their TAP-3 Elite and exits the study, whereupon he/she becomes a routine WRNMMC OSA patient.

The participant's total time involved in the study is estimated to be on the order of 12-14 weeks. Upon re-entering the normal WRNMMC care protocol, the participant receives routine follow-up care for the TAP-3 Elite by the primary dental care provider at their yearly

follow-ups. They should be followed up by their sleep physician every 3-4 years. Although each individual's participation will involve about 12-14 weeks, the study will last approximately 12-18 months as there will be only a few participants actively in titration at any one time. After all 20 subjects complete the protocol, analysis of data begins (See APPX N).

Data collection and analysis

During the course of the study, there will be two principle sources of data. First, there is the data collected from the participants during the initial diagnostic PSG. Once a participant is accepted into the study and consent is given, data records will be provided to the Principle Investigator (PI). Data will include initial AHI and ODI from the PSG and the ODI from the VirtuOx pulse oximeter. The sleep laboratory data base is not connected to the WRNMMC intranet. Therefore investigators will retrieve these data from the data base in chronological order during the time frame the study is conducted. Collecting this data set is part of the established sleep lab procedure and will not require using any study investigators. Investigators will use patient identifiers and date of initial sleep study to retrieve initial sleep study AHI, ODI from the PSG and the ODI from the VirtuOx pulse oximeter, ESS and FOSQ scores and demographic data (age, weight, height, gender and ethnicity). After the post titration sleep study AHI, ODI from the PSG and the ODI from the VirtuOx pulse oximeter, ESS and FOSQ scores will be obtained. These data will be placed in participant's data file marked only by study number.

The second source is data from the 20 participants enrolled in the home-titration protocol. When participants are consented in the Orofacial Pain Center they will complete the ESS, PSQI and PSS subjective questionnaires and have maximum jaw opening and protrusion measurements recorded. These will be repeated when patients return after titration. During the titration period, VirtuOx Inc. pulse oximetry data will be securely uploaded to the cloud and then be downloaded and placed in individual study files. These data include basal SpO2, ODI, Pulse, Awake SpO2, High SpO2 and Low SpO2. In addition, each participant is maintaining two daily logs; one will contain 0 to10 VAS to record end of day stress and sleep quality and any jaw pain upon waking. The second daily log tracks wearing the MAD during the first week at 60% maximum protrusion, and then verifies MAD adjustments during self-titration as changes in mandibular protrusion are made. These logs will be collected at the end of the titration period before the participant goes for the post titration PSG one week later. Pulse oximetry data will be correlated, by date, with subjective measures in the daily logs and the objectives measures of jaw protrusive settings that the participants set on their MAD (See APPX O).

Data and Privacy Protection

As each participant is enrolled, they will be given a study ID number (1 to 20) based on the chronology of their enrollment. A master list, kept on the secure hard drive of the primary investigator's (PI) locked office, will associate subject name, last four of their social security number, telephone number, email address and date of study enrollment with the study ID number. Only the PI will have access to the master list on the hard drive. A paper copy of

the master list will be kept in the PI's locked office and will only be used by investigators to collect data from the diagnostic and post titration PSG. After data collection the paper copy of the master list will be destroyed. The hard drive copy will only be checked for contact data in case a subject must be contacted due to scheduling problems, or some new information is learned that a subject needs to know, or if a subject at the end of the study wants to know about their data.

The study ID number will identify all data collection sheets, daily logs and individual data files. ESS, PSQI and PSS will be marked by the study number. The data from the diagnostic and post-titration PSG in the Sleep Disorders Clinic are identified by patient name and will be retrieved and placed in paper data collection sheets marked by the participant's study number. These paper data collection sheets and questionnaires will be placed in individual data files stored in a locked cabinet in the PI's office. These data will be transcribed into master summary data sheets on the secure desk top computer in the PI's locked office. Signed Informed Consent and HIPAA forms will be kept in a locked file in the PI's office. Each subject will be given a copy of the signed Informed Consent and HIPAA forms.

Subject initiated contacts via phone or email to the PI with respect to adverse events, side effects or questions will be recorded on an electronic log. The log will contain the call date and time, the nature of the question and response as well as any ancillary information necessary to clarify the contact. The log will be maintained by the PI on a desktop computer located in a locked office.

VirtuOx pulse oximetry data will be identified by the study number and patient initials and uploaded to the cloud. These objective measurements will be calculated for each participant and be posted weekly on VirtuOx, Inc's HIPAA-compliant server for access by the investigators. These data will be compared by date to protrusive setting and subjective measures.

The VirtuOx pulse oximeter is a high resolution instrument, recording the percentage of oxygen saturation in the peripheral blood every second. This sample rate is more than sufficient to accurately detect a blood oxygen de-saturation event which is partly defined as having a duration of 10 seconds or more. ODI is also defined as a drop in SpO2 of more than 3% below a 2 minute running average. The web server has cloud-based software that calculates the ODI and can display continuous SpO2 with individual desaturation events highlighted, as well as summary ODI scores. The raw data as well as the derived results are stored on VirtuOx Inc.'s HIPAA-compliant server and the PI obtains secure access with a password.

Summaries of ESS, FOSQ, PSQI, PSS

ESS is a widely used subjective measure in sleep medicine. It effectively discriminates between normal subjects and those with significant sleep disturbances. It has a high level of reliability (r=.82) and internal consistency as measured by Cronbach's alpha (0.88) (Johns, 1991). The ESS is self-administered, consisting of eight questions. It asks patients to rate

how likely they would fall asleep in various daily situations, using a pseudo-analog scale ranging from 0 = "never doze" to 3 = "high chance of dozing". The scores of the eight questions are summed. Normal subjects have a mean score of 5.9 while OSA patients score significantly higher with a mean of 11.9 (Johns, 1991). The AASM recommends the ESS as part of the OSA diagnostic process (Epstein et al., 2009). See Appendices B and C for details.

FOSQ is a self-administered, disease specific quality of life questionnaire that consists of 30 items with 5 subscales. It determines functional status in adults by assessing the impact of excessive sleepiness disorders on multiple activities of everyday living and the extent to which these abilities are improved by effective treatment. The domains it covers are activity level, vigilance, intimacy and sexual relationships, general productivity, social outcome, and the difficulty of performing a given activity. A 4-point scale is used. FOSQ scoring test-retest reliability value is alpha (α) = 0.90 and the scoring internal consistency is $r = 0.90$. An available shorter version, the FOSQ 10, has similar validity and reliability to the FOSQ with an internal consistency of $\alpha = 0.87$. It is available in multiple languages as well as English (Weaver et al., 1997). See Appendices D and E for details.

PSQI is a self-report instrument that accesses sleep quality and disturbances over the last month (Buysse et al., 1989). It uses 19 questions to collect sleep information that describe a patient's sleep quality, latency, duration and efficiency. A global PSQI score greater than 5 yielded a diagnostic sensitivity of 89.6% and specificity of 86.5% (kappa = 0.75, $p < 0.001$) in distinguishing good and poor sleepers (Buysse et al., 1989). Another study of bone

marrow transplant patients, renal transplant patients, women with breast cancer and women with benign breast problems demonstrated Cronbach's alphas of 0.80 across groups. Correlations between global and component scores were moderate to high and PSQI scores were moderately to highly correlated with measures of sleep quality and sleep problems (Carpenter & Andrykowski, 1998). Another study showed that a PSQI global score > 5 resulted in a sensitivity of 98.7% and specificity of 84.4% for sleep disturbances in insomnia patients versus controls, and the overall PSQI global score correlation coefficient for test-retest reliability was 0.87 (Backhaus et al., 2002). Other work shows that the PSQI has internal consistency and a reliability coefficient (Cronbach's alpha) of 0.83 for its seven components. It has been translated into 56 languages (Smyth, 2012). See Appendices F and G for details.

PSS is a 10-item self-report questionnaire that measures how a person evaluates the stressfulness of situations in the past month of their lives (Cohen, 1988). The PSS was designed for use with community samples with at least a junior high school education. The items are easy to understand and the response alternatives are simple to grasp. The PSS is an empirically established index of general stress appraisal that "measures the degree to which situations in one's life are appraised as stressful". Early on, it was demonstrated to have an internal reliability coefficient alpha of 0.78, and construct validity based on stressful event frequency, predictive validity for biological disease and discriminate validity for showing that perceived stress is associated with greater clinical illness (Cohen et al., 1993). Recent work in asthma patients showed Cronbach's alpha coefficients for negative factor, positive factor and total score were 0.86, 0.83, and 0.90, respectively (Maroufizadeh et al., 2014).

See Appendices H and I for details.

Pulse Oximeter

VirtuOx, Inc will provide portable pulse oximeters and the web-based data uploading, storage, and cloud-based data analysis (See APPX Q). VirtuOx, Inc is a privately held medical technology services company that provides diagnostic tools and services that enable a variety of healthcare organizations and professionals to diagnose and treat respiratory diseases through vertically integrated platforms, products and services. The VirtuOx, Inc platforms include a Medicare approved, Joint Commission Accredited Independent Diagnostic Testing Facility (IDTF) that assists in the diagnosis for Sleep Disorder Breathing and Respiratory Diseases at home. They also have web-based data management applications. VirtuOx, Inc has a commercially available software program to analyze oxygen saturation (SpO2) records and derive the ODI from this data.

This is an ideal system for the screening of patients while at home since the data is uploaded to the cloud in a secure manner and can be accessed by the investigators or clinicians. Oxygen saturation is sensed by a probe worn on a finger while the processor and transmitter can be placed near the patient. The VirtuOx, Inc pulse oximeter generates an SpO2 signal every second and relays this wirelessly to the cloud. This is rapid enough to meet the definition of ODI (shift of more than 3%-4% for 10 seconds).

Role of Government Organizations

The WRNMMC Sleep Disorders Clinic will make the OSA diagnosis using current standard procedures. They have agreed to add the use of a wireless VirtuOx portable pulse oximeter to allow simultaneous collection of ODI from both a type 4 instrument and their type 1 instrumentation during both diagnostic and post-titration PSG sessions. The WRNMMC information Technology Dept. and the Sleep Laboratory personnel are currently working with VirtuOx to resolve connectivity engineering issues.

NPDS Orofacial Pain Center investigators will clinically deliver the TAP-3 Elite MAD. The Airway Management Company is the manufacturer of the mandibular advancement device, the TAP-3 Elite, proposed for this study. This oral appliance is currently preferred for OSA treatment by WRNMMC and NPDS. The cost of the TAP-3 will be covered by the NPDS/Orofacial Pain clinical operations budget. NPDS Prosthodontics lab will complete laboratory manufacture of the TAP-3.

NPDS will lead the analysis of the data in cooperation with investigators from the WRNMMC sleep clinic and VirtuOx, Inc. Anticipated study duration for each participant is about 3-4 months. It will take about 18 months to complete the entire 20 person study.

Standard of Care

The standard of care used in this study will be the same as is currently practiced by the

Orofacial Pain Clinic. Specifically, the home-titration of the MAD using subjective assessment of sleep quality and jaw comfort will be conducted to determine optimum protrusion length. Participants will adjust the MAD to protrude their mandible 0.25 mm every other night if tolerable. The MAD being used is the TAP-3 Elite which is routinely used at WRNMMC and NPDS. The ESS, FOSQ and a daily diary using VAS for sleep quality, any jaw pain, and stress will be employed. Additionally, the PSQI and PSS part of the standard of care at the Orofacial Pain Center will also be administered. These data will be compared with nightly ODI readings as part of the research. After home-titration, a second PSG will be conducted at the sleep laboratory to assess the efficacy of the protrusive setting on the MAD to lower AHI. Visits for the MAD delivery and adjustments prior to the post-titration PSG are in line with the standard of care for MAD treatment.

Current Status of Research Project

The preliminary design for this Pilot Study has been under development since August 2014. An early release of the VirtuOx wireless pulse oximeter was tested in the WRNMMC sleep lab and found to be incompatible. There are cellular internet networking obstacles in this facility due to the shielding in the lab. The WRNMMC sleep lab has minimal cellular connectivity to the internet cloud and thus our pulseox device cannot yet be tracked well. The WRNMMC IT Department and VirtuOx are working to find a solution.

When issues are resolved, the study design and protocol will be finalized. A Cooperative Research and Development Agreement (CRADA) between VirtuOx and WRNMMC will be finalized and all plans submitted to the Institution Review Board (IRB).

A meeting with Geneva Foundation will take place next month to discuss the content of the CRADA.

CHAPTER IV: RESULTS

A clinical trial has been designed to create the first real time data set that tracks ODI on a nightly basis during home-titration of MAD therapy for OSA patients. This could help a dentist to objectively titrate a MAD. Objective data will suggest how jaw protrusion and ODI vary in relation to more traditional subjective measures such as perceived stress, jaw pain and nightly sleep quality. A request for study approval has been prepared for submission to the IRB, who must approve the study protocol before the trial can begin.

The data will relate ODI to AHI in the diagnostic PSG and post-titration PSG. This large data set on 20 patients should allow sample size determination for a definitive study that shows what degree of protrusion achieves optimal ODI measures and improved OSA symptoms.

VirtuOx Inc. has joined with the NPDS to pursue this topic and a CRADA between VirtuOx and WRNMMC via Geneva Foundation is in discussion. VirtuOx has committed to development of a version of its wireless pulseox technology that would maintain connectivity with its cloud server even in difficult locations such as the WRNMMC sleep laboratory.

All subjective data instruments have either been designed by the Orofacial Pain Department, or permission has been obtained from the copyright owner.

CHAPTER V: DISCUSSION

Although millions of people suffer from OSA only a small percentage receive treatment due to two factors; lack of disease awareness and the high cost of diagnosis and treatment. CPAP opens the airway by using air pressure to push the soft tissue of the upper airway away from the collapsed position. Alternatively, a MAD pulls the mandible and tongue anatomy forward to open the upper airway somewhat like the jaw thrust maneuver in cardiopulmonary resuscitation. While not as universally effective as a CPAP in reducing AHI, compliance with MAD is higher than for CPAP.

In a sleep laboratory during the PSG, a sleep technician titrates CPAP pressure while monitoring the patient's quality of sleep. This titration process does not disturb the patient and is done in one night to minimize costs. However, in a sleep lab MAD titration to lower AHI involves repeated mechanical adjustments of the device that will likely wake the patient. Remotely titrated MADs (jaw advancement adjusted electrically from another room) are still experimental, and FDA approved commercial models are not available.

Alternatively, a patient can adjust a MAD at home to achieve the most clinically beneficial mandibular position. Home treatment with MADs has been typically monitored through subjective questionnaires filled out by the patient, and sometimes a bed partner as well. Adding a portable pulse oximeter to monitor blood oxygen levels provides objective data about sleep quality during home MAD titration. Research suggests that simultaneous use of

both objective and subjective measures may achieve a more accurate titration end point. MADs will never fully replace CPAP, particularly, in patients with severe OSA. However, for mild and moderate OSA, and perhaps even in some patients with severe OSA, a MAD adjusted to "optimum" protrusive position can be nearly as effective as CPAP at lowering AHI. MADs are more convenient than CPAP and are used on a more regular basis than CPAP. Unfortunately, a consensus as to what constitutes "optimum" protrusive mandibular position has not been established. Nor has it been demonstrated how both objective and subjective data determine the most optimal jaw setting during home MAD titration.

An objective and subjective data set is needed to demonstrate how a home titration protocol could optimize the clinical outcomes achieved by MADs. Such data could enhance the quality of OSA treatment for a much larger population at lower cost and greater convenience. This research proposal takes a step towards establishing a standard process to demonstrate how optimum home titration of MADs for OSA treatment may be achieved.

Participants with mild to moderate OSA will slowly advance the mandible to a protrusion setting that does not cause discomfort and maximally inproves sleep quality based on subjective measures. Participants will wear a VirtuOx, Inc. portable pulse oximeter to monitor ODI at the diagnostic PSG, during home titration, and at the post MAD titration PSG. The titration period will allow participants to reach, if needed, their maximum protrusion as governed by the traditional subjective measures. During home titration, nightly ODI data, protrusive jaw settings, and standardized subjective data will be tracked. At the post home titration PSG, the sleep technician will not adjust the MAD. ODI will be

correlated to the protrusive settings as well as with ESS, FOSQ, PSQI, PSS, snoring, VAS for stress, discomfort and sleep quality and the diagnostic and post titration AHIs from PSG. This data set of the subjective findings with nightly measures of protrusion and ODI may identify how ODI indicates when optimal titration of a MAD occurs.

SIGNIFICANCE OF RESEARCH

If the ODI measures in this study compare favorably with the AHI from diagnostic PSGs and post MAD titration PSGs, then pulse oximetry data could be considered a reliable indication of relative efficacy of the MAD treatment during and after titration. With sufficient clinical testing of this protocol, the need for expensive follow-up PSG sessions in a sleep lab can be avoided.

The working premise of this approach is that the ODI derived from a type 4 instrument will not be the basis of a diagnosis of OSA but rather it can be used as an indicator of the treatment efficacy trend as the titration proceeds. Since only a close trending association between AHI and ODI is required for this approach, absolute correlation between the two measurements is not required. The technology to enable trained dental caregivers to remotely administer this protocol, even for deployed military personnel, is rapidly becoming available. The cost reduction potential for the healthcare community is significant since the majority of OSA patients are good candidates for this treatment approach. Monitoring ODI via the cloud would cost one hundred dollars per MAD home

titration as opposed to fifteen hundred dollars for the post-titration PSG now currently used to confirm a reduced AHI.

Pulse oximetry data uploaded to the cloud would allow real time assessment of a patient's oxygen saturation during home titration. Providers could advise patients on a real time, daily basis. Because the data is collected electronically, appointments and lost work days could be reduced.

PATIENT EXPERIENCE

The pulse oximetry data for ODI in this study can be instantly downloaded from the patient's home to the dental or medical office via the cloud in order to guide MAD titration. Patients only need to wear and turn on the device and periodically charge the battery. They do not need a computer nor bring a chip to the office. The data from this study may set a standard for the demand that a simpler, more clinically- and cost-effective MAD titration protocol be established (Bailey, 2011; Gauthier et al., 2012). This data would also provide a baseline for randomized clinical trials that could compare MAD home titration protocols using the traditional subjective measures to those using subjective measures and pulse oximetry and thus support this approach with valid science-based proof of efficacy.

Participants in this study will experience no more risks than patients diagnosed with mild to moderate OSA who are being treated with a MAD using current standard practice at WRNMMC. Side effects usually are minimal and almost always transient. Commonly

reported minor and temporary side effects for MADs include transient TMJ pain, muscle pain, tooth pain, salivation, TMJ sounds, dry mouth, gum irritation, and morning-after occlusal changes. Severe and continuous side effects are very rare and, if they occur, present as more intense aspects of the previously listed items.

By participating, the subjects may contribute to society. The data may help develop a standard of care protocol that will make future OSA treatment with MADs more effective by shedding light on how to:

- achieve optimal jaw protrusion to open the airway
- reduce the need for sleep laboratory post titration PSG assessments

Subjects in this study may benefit because they will be provided standard OSA therapy, be monitored by objective measures of AHI and ODI, and will have access after the study to their data and how it affected the use of their MAD. The study subjects will keep their TAP-3 Elite appliances to treat their OSA. The TAP-3 Elite is an oral appliance approved by the FDA.

Active duty military members will benefit from this research because this data may support treatment that allows service members with OSA to be deployed with a MAD and pulse oximeter. The data provided by pulse oximetry will allow MAD adjustments even in a stress inducing environment that can maintain a reduced AHI and optimum protrusion.

CHAPTER VI: CONCLUSIONS

No previous study has tracked nightly ODI for correlations with AHI, subjective measures, and jaw protrusion. This work has designed a pilot clinical trial that should validate the science of the titration approach outlined in this research. Once validated, this scientific approach can be used as the methodology in a full-scale clinical trial that would establish the use of ODI in objective data-guided titration of MADs for optimum jaw protrusion.

APPENDIX A

DENTAL SLEEP MEDICINE EXAM FORM

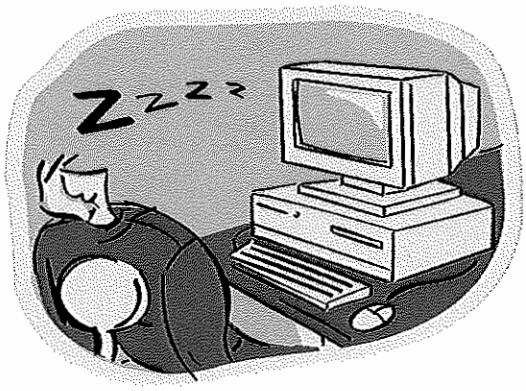
Orofacial Pain Center
Naval Postgraduate Dental School

8901 Wisconsin Ave

Bethesda, MD 20889

(301)295-1495

FAX (301)295-2070



Dental Sleep Medicine Exam Form

FEB 2013

Please complete pages 1 through 8.

Circle choices whenever available.

Name _____
Date_____

Sponsor SSN _____ DOB _____ Gender:
M F

Active Duty / Retired / Family member Age_____
Ethnicity_____

Branch of Service _____ Rank / Rate _____

Phone (H) (____)_____ (W) (____)_____ (Cell) (___)_____

Address _____

City _____ State _____ Zip _____

Email _____

Are you enrolled in? TRICARE Prime TRICARE Extra TRICARE Standard Medicare

Do you have other Insurance? Y N Insurance Company _____

Insurance Policy Number_____

Who referred you for this evaluation?

_____

Name _____

BP ____/____

Pulse _____

O_2 Sat _____%

Height _____

SLEEP HISTORY

Why are you here? Describe your sleep problem(s):

When did your problem(s) start? _____

Who have you seen before for this problem? _____

1. What position do you fall asleep? Back Side Stomach

2. Do you have a consistent sleep schedule? Y N Are you a shift worker? Y N

3. How many hours do you sleep? Average night ____ Good night ____ Bad night ____

4. How long does it take to fall asleep? Average night ____Good night ___Bad night___

5. Do you have difficulty falling asleep? Y N _____

6. Do you have difficulty staying asleep? Y N _____

* What may interrupt your sleep? _____

7. Do you snore? Y N _____

8. Do you hold your breath or gasp for air while sleeping? Y N_____

9. Is your sleep? sound light restless _____

10. Do you have nightmares? Y N How often? _____

11. Is your sleep restorative/ restful? Y N _____

12. Have you had a sleep study in the past 12 months? Y N _____

To be completed by staff	
Date of PSG:	
AHI:	RDI:
O_2 Sat:	Sleep Eff%
Sleep latency:	Time is stage N3 (III/IV):
Other:	

13. How have you managed your sleep issues in the past? _____

14. Have you used an air mask to manage your sleep apnea before? Y N N/A

What was your experience with this/ side effects?

_____

15. Have you used an oral appliance to manage your sleep apnea before? Y N N/A

What was your experience with this/ side effects? _____

_____

Do you use any of the following sleep aids? (Circle all that apply)

Ambien Lunesta Trazodone Benadryl Tylenol PM Melatonin

Alcohol Other _____

What is the dose?_____ How soon before bed do you take this? ____

How many days per week do you use this? _____

How long have you been using this? _____

How well does this work? Good Fair Poor

What sleep issue(s) has any provider diagnosed you with? (Circle all that apply)

Sleep apnea Insomnia Snoring Restless legs syndrome Tooth grinding

Narcolepsy Sleepwalking Sleep talking Sleep eating Sleep terrors

Other: _____

Other sleep information (Circle all that apply)

1. With the lights out, is your bedroom…
   Too bright Too dark Just right

2. The temperature of your bedroom is…
   Too warm Too cold Just right

3. The environment around your bedroom is…
   Too noisy Just right Too quiet

How sleepy are you? How likely are you to doze off or fall asleep in the following situations, in contrast to feeling just tired? This refers to your usual way of life in recent times. Even if you have not done some of these things recently try to work out how they would have affected you. Use the following scale to choose the most appropriate number for each situation:

0 = no chance of dozing
1 = slight chance of dozing
2 = moderate chance of dozing
3 = high chance of dozing

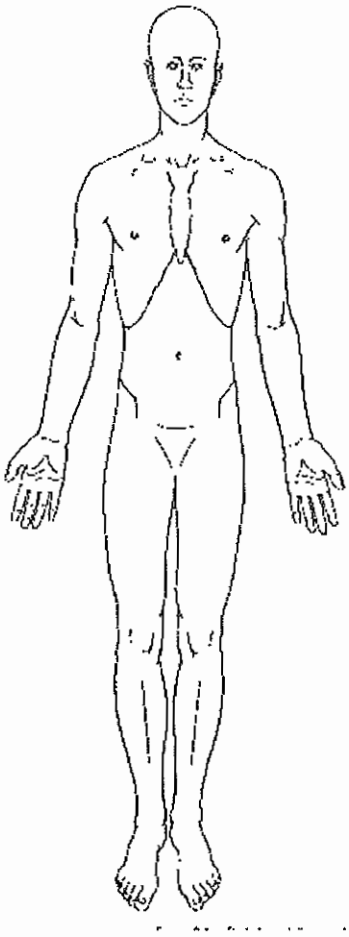
SITUATION	CHANCE OF DOZING
Sitting and reading	_____
Watching TV	_____
Sitting inactive in a public place (e.g a theater or a meeting)	_____
As a passenger in a car for an hour without a break	_____
Lying down to rest in the afternoon when circumstances	_____

permit	
Sitting and talking to someone	_____
Sitting quietly after a lunch without alcohol	_____
In a car, while stopped for a few minutes in traffic	_____

TOTAL SCORE _____

PAIN HISTORY:

Draw the location(s) of ANY pain that you experience.



Circle which word(s) characterize your pain or pains?

Sharp Burning Electric-like Aching Throbbing Dull Pulsing Pressing Stabbing

What is the level of pain/tension to the head & neck? (Mark your levels on the lines below).

List your pain problems.

Prioritize (worst pain first)

1. _____

2. _____

3. _____

4. _____

5. _____

Which pain occurred first?

_____

Does movement initiate or aggravate your pain? Y N ?

_____

No discomfort Worst pain imaginable

Today 0_____10

At its Worst 0_____10

On Average 0_____10

Pain on Best day 0_____10

Any pain free days? Yes No How many pain free days per month? _____

When were you last completely pain free?

_____

What is the level of pain/tension to the rest of the body? **(Mark your levels on the lines below).**

No discomfort Worst pain imaginable

Today 0_____10

At its Worst 0_____10

On Average 0_____10

Pain on Best day 0_____10

Any pain free days? Yes No How many pain free days per month? _____

When were you last completely pain free?

_____

Please rate your overall levels of:

	None	Worst possible
Stress	0	10
Anxiety	0	10
Depression	0	10
Anger	0	10

Have you ever thought of harming yourself? Yes No _____

Estimate in hours, for any reason, how long your teeth are together or touching in a 24 hour period? _____hours

Circle the feeling(s) that let you know when your teeth are touching?

pain tightness fatigue motion touch

Do you clench or grind your teeth? Yes No Don't know

If yes, how do you know? self-aware told by dentist told by others

Habits. Do you? (Circle all that apply)

biting nails chew gum hold the tongue to the roof of the mouth protrude the tongue hold phone between shoulder & head

Describe any other habits: _____

MEDICAL & DENTAL HISTORY

a. Medical Conditions:

_____

_____

b. Allergies: _____

c. Current prescription medications: _____

_____

d. Herbal/Dietary Supplements: _____

e. Current non-prescription medications: _____

f. When was your last dental check up? _____

g. Do you have any dental work required that has not yet been completed? Yes No

If yes, please explain _____

h. Do you have a history of headaches? Y N

Location of headache (s): _____

Do you wake up with headaches? Y N

Do you experience any of the following?

a. Jaw pain/stiffness ? Y N
Is this worse in the morning mid day evening varies

b. Tooth pain? Y N _____

c. Does your bite feel different? Y N _____

d. Any altered jaw movement(s)? Y N _____

e. Any jaw (joint) sounds? Y N _____

j. When were you first aware of the jaw sounds? _____

k. Have there been any changes in the jaw sounds?_____

l. Any jaw pain or stiffness? Y N morning midday evening _____

m. Does your problem affect your ability to eat? Y N _____

n. Do you have ear symptoms Y N pain ringing fullness muffled hearing

What is your consumption of the following?

Nicotine Y N cigarettes _____/day cigars_____ pipe _____ snuff _____

Alcohol Y N beer _____/day wine _____ glasses/day liquor ____drinks/day

Caffeine Y N cups(cans)day _____ coffee tea soda chocolate

Water Y N glasses/day _____

Juice or milk Y N glasses/day _____

Is your diet? balanced high sugar high carbohydrate high fat

Do you skip any meals? Y N Which? Breakfast Lunch Dinner

Any recent weight gain/loss? _____

Personal/Family History

a. Occupation: _____

b. Do you have a history of the following or other similar threatening, stressful or frightening life events? Abuse, at any age (physical, emotional or sexual), childhood neglect, physical or sexual assault, near drowning, panic attacks, post-traumatic stress disorder, deployment to a conflict zone, a significant motor vehicle accident? Y N
Other:_____
_____

c. Exercise level: None Slight Moderate Active

Any activity limitations:_____

_____

Thank you. The staff will complete the remainder of the form.

EXAMINATION

CN SCREENING EXAM

(I-XII): WNL Finding(s): _____

Not assessed

CERVICAL EXAM

Head/ Neck Position _____ WNL: Forward Head/body Tilt/turned R L

Rounded shoulders _____

Neck circumference: _____ inches

Cervical ROM with or without pain: _____

_____

_____

RANGE OF MANDIBULAR MOTION

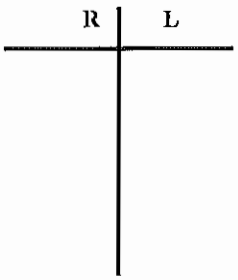
Incisal opening:	without increasing pain	____ mm	Pain level ____
	maximum unassisted	____ mm	Pain level ____
	maximum assisted	____ mm	Pain level ____

Location of pain _____

Is there pain on?

Right Lateral Movement ____ No ____ Yes, ____ R ____ L _____ mm

Left Lateral Movement ____ No ____ Yes, ____ R ____ L _____ mm



Protrusive Movement ____ No ____ Yes, ____ R ____ L _____ mm

Any Deflection / Deviation Y N R L _____mm

End Feel (with restriction) Hard Soft

Overbite: _____ mm Overjet: _____ mm

TMJ SOUNDS

Crepitus: None Right Left Mild Moderate Severe

Click or Pop: None Right Opening Reciprocal Intermittent Painful

None Left Opening Reciprocal Intermittent Painful

Is sound eliminated with protrusion? _____ No _____ Yes

CLENCHING TEST

Is there pain when clenching on posterior teeth? ____ No ____ Yes R L

Clenching on tongue blades is?

Bilateral:	Better	Same	Worse	R or L
Right:	Better	Same	Worse	R or L
Left:	Better	Same	Worse	R or L

PALPATION

Codes: 0 = Non Painful, 1 = Tenderness, 2 = Painful, 3 = Pain with withdrawal

T = Trigger Point (draw arrow to depict pattern of referral, if present)

A = allodynia, H = hyperalgesia ↑ = hypertrophy ↓ = atrophy

	Right	**Left**
Rhomboids	_____	_____
Lev Scap	_____	_____

Trapezius _____ _____

SCM _____ _____

Splenius _____

_____

Occipital _____ _____

Paracervical _____ _____

C Spine _____

Masseter _____ _____

Temporalis _____ _____

Frontalis _____

_____

TMJ (static) _____ _____

TMJ (dynamic) _____ _____

TMJ (EAC) _____ _____

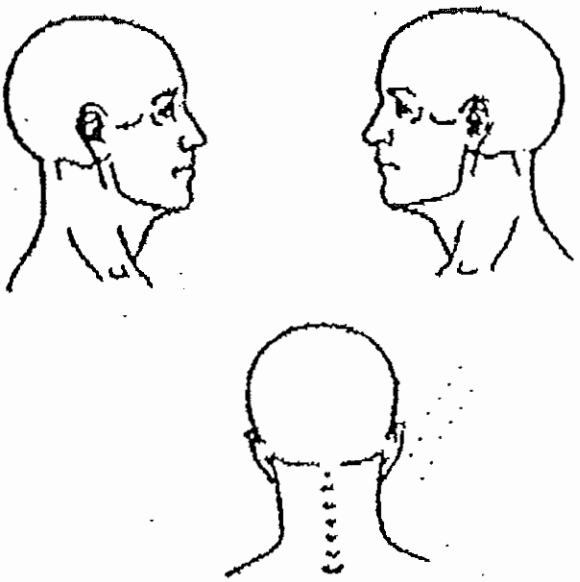
Lat Ptery _____ _____

Joint Loading _____ _____

Temp Tend _____ _____

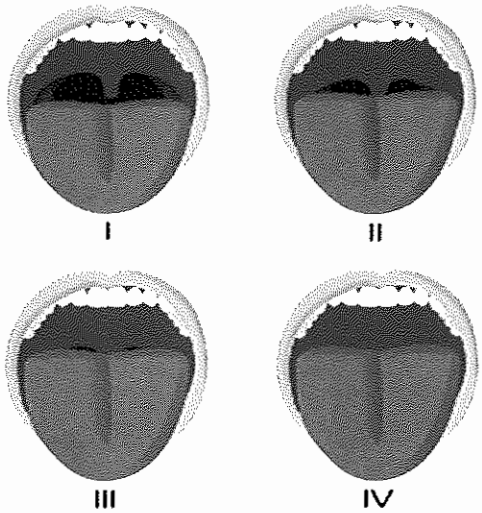
Med Ptery _____ _____

Digastric _____ _____



ORAL EXAM

Mallampati Classification: _____



Acute malocclusions? _____ No _____ Yes Location/when? _____

Soft Tissue _____ WNL: _____

Periodontal Health: _____ WNL: _____

Tooth sensitivity/percussion:_____

General description of the dentition:

_____

Tooth Wear: Physiologic ____ Moderate ____ Severe ____

Mandibular posturing / tongue thrusting? Y N _____

Occlusion: Is the occlusion stable? Y N _____

Angle Classification: I ____ II ____ Div 1 2 III ____

Open Bite? Y N _____

Guidance/Interferences?

_____

Splint History: _____

Are there enough teeth for OAT? Y N

- i.e. at least 6 teeth per arch to include one posterior tooth per quadrant

IMAGING

Radiographs/ Imaging: _____ Not Indicated

____ Panoramic _____

____ TMJ Series _____

____ Intraoral _____

____ CT Scan _____

____ MRI _____

____ Other _____

MANAGEMENT PLAN

___ Sleep hygiene

___ Sleep diary

___ Nutritional counseling/ weight mgmt

___ MAD (mandibular advancement device) therapy

Appliance of choice: _____

___ Sleep Medicine referral

___ Rx Hypnotic

___ Other: _____

ABDSM board criteria

Date Eval	Gender	Age	Race

Pre-treatment numbers

AHI	O2 Sat	ESS	OSA severity

Post-treatment numbers

AHI	O2 Sat	ESS	OSA severity

Procedure	CPT Code	Cost	
New patient, expanded (20)	99202	$123	
New patient, moderate complexity (45)	99204	$227	
New patient, high complexity (60)	99205	$307	
Established patient, expanded (15)	99213	$95	
Established patient, detailed (25)	99214	$137	
Established patient, comprehensive (40)	99215	$219	
Observation/inp hospital care (25)	99232	$123	
Observation/inpt hospital care (45)	99234	$231	
Office consultation, brief (15)	99241	$139	
Office consultation, expanded (30)	99242	$177	
Office consult, comprehensive (60)	99244	$295	
Office consult, complex (80)	99245	$372	
Special reports (insurance, boards)	99080	$56	
Medical team conference (30)	99361	$136	
Medical team conference (60)	99362	$237	
Telephone call, 5-10 min	99371	$22	
Telephone call, 11-20 min	99372	$54	
Telephone call, >21 min	99373	$108	
Prolonged service w/o contact	99358	$118	
Prolonged service w/o contact ADD	99359	$61	
Injection, tendon shealth/ligament	20550	$64	
Trigger point injection (1 or 2)	20552	$60	
Trigger point injection (3 or more)	20553	$67	
Muscle testing, extremity or trunk	95831	$33	
Range of motion measurements	95851	$20	
Biofeedback training, any modality	90901	$109	
Application: hot or cold packs	97010	$27	
Application of electrical stim	97032	$37	
Manual therapy, myofascial release	97140	$31	
Prevent. med. ind. counseling (15)	99401	$52	
Exercises, develop range of motion	97110	$33	
Neuromuscular reeducation, posture	97112	$35	
Acupuncture, W/O stim., 15 min	97810	$56	
Acupuncture, W stim., 15 min	97813	$61	
Acupuncture, W stim., ADD 15 min	97814	$52	
Acupuncture, W/O stim., ADD 15 min	97811	$46	

Procedure	ADA Code	Cost	
Detailed, extensive evaluation	D0160	$171	
Problem focused re-evaluation	D0170	$57	
Consultation	D9310	$101	
Pall (Emerg) Tx: Dental pain	D9110	$100	
Local anesth not in conj w opr/surg	D9210	$41	
Theraputic drug injection	D9610	$76	
Pulp vitality tests	D0460	$47	
Behavioral management (1/15 min)	D9920	$40	
Nutrition counseling	D1310	$46	
Tobacco counseling	D1320	$50	
Individual OHI	D1330	$64	
Other drugs/meds	D9630	$40	
Occlusal orthotic device	D7880	$696	
Athletic mouth guard	D9941	$147	
Repair/reline occlusal guard	D9942	$157	
Occlusal adjustment limited	D9951	$111	
Diagnostic casts	D0470	$104	
Oral/facial photography	D0350	$59	
Patient seating	A9999	$0	
Imaging			
Panorex	D0330	$110	
Intraoral, first film	D0220	$27	
Intraoral, each add. film	D0230	$24	
Occlusal	D0240	$41	
Nurse			
Telephone call, 5-10 min	98966	$11	
Telephone call, 11-20 min	98967	$23	
Telephone call, >21 min	99443	$35	

Wounded warrior: Yes No

Co-morbidities:

Abuse Combat TBI PTSD Panic Disorder

GERD IBS FM Inter Cyst Vulvo OSA

Diagnosis: (Number 1 – 5 as applicable, where 1 is the primary diagnosis)

Atypical facial pain

Neuropathy, neuropathic

Trigeminal nerve disorder

Disorders of other cranial nerves

Cluster Headache

Headache

Hemicrania

Migraine with aura

Migraine without aura

Tension type headache

Myalgia

Cervical MFP

Masticatory MFP

Non-neutral head and neck posture

Protective co-contraction

TMJ arthralgia

Disc displacement with reduction

Disc displacement without reduction

Osteoarthritis

Subluxation

Sleep apnea

Sleep disturbance

Sleep disorder

Bruxism

Cervicalgia

Fibromyalgia

Otalgia

Reaction to chronic stressors

APPENDIX B

EPWORTH SLEEPINESS SCALE

How sleepy are you? How likely are you to doze off or fall asleep in the following situations, in contrast to feeling just tired? This refers to your usual way of life in recent times. Even if you have not done some of these things recently try to work out how they would have affected you. Use the following scale to choose the most appropriate number for each situation:

0 = no chance of dozing
1 = slight chance of dozing
2 = moderate chance of dozing
3 = high chance of dozing

SITUATION	CHANCE OF DOZING
Sitting and reading	_____
Watching TV	_____
Sitting inactive in a public place (e.g a theater or a meeting)	_____
As a passenger in a car for an hour without a break	_____
Lying down to rest in the afternoon when circumstances	_____

permit	
Sitting and talking to someone	_____
Sitting quietly after a lunch without alcohol	_____
In a car, while stopped for a few minutes in traffic	_____

TOTAL SCORE _____

APPENDIX C

SCORING INSTRUCTIONS FOR EPWORTH SLEEPINESS SCALE

The Epworth Sleepiness Scale

The Epworth Sleepiness Scale is widely used in the field of sleep medicine as a subjective measure of a patient's sleepiness. The test is a list of eight situations in which you rate your tendency to become sleepy on a scale of 0, no chance of dozing, to 3, high chance of dozing.

When you finish the test, add up the values of your responses. Your total score is based on a scale of 0 to 24. The scale estimates whether you are experiencing excessive sleepiness that possibly requires medical attention.

How Sleepy Are You?

How likely are you to doze off or fall asleep in the following situations? You should rate your chances
of dozing off, not just feeling tired. Even if you have not done some of these things recently try to determine how they would have affected you. For each situation, decide whether or not you would have:

- No chance of dozing =0
- Slight chance of dozing =1
- Moderate chance of dozing =2
- High chance of dozing =3

Write down the number corresponding to your choice in the right hand column. Total your score below.

Situation Chance of Dozing

Sitting and reading
Watching TV
Sitting inactive in a public place (e.g., a theater or a meeting)
As a passenger in a car for an hour without a break
Lying down to rest in the afternoon when circumstances permit
Sitting and talking to someone
Sitting quietly after a lunch without alcohol
In a car, while stopped for a few minutes in traffic
Total Score = _____

Analyze Your Score
Interpretation:
0-7: It is unlikely that you are abnormally sleepy.
8-9: You have an average amount of daytime sleepiness.
10-15: You may be excessively sleepy depending on the situation. You may want to consider seeking medical attention.
16-24: You are excessively sleepy and should consider seeking medical attention.
Reference: Johns MW. A new method for measuring daytime sleepiness: The Epworth Sleepiness Scale. *Sleep*
1991; 14(6):540-5.

This printed version of the Epworth Sleepiness Scale is provided courtesy of Talk About Sleep, Inc.

www.talkaboutsleep.com.

APPENDIX D

FUNCTIONAL OUTCOME OF SLEEP QUESTIONNAIRE

Site: _____ ID #: _____
Date of Data Entry: _____ Trial _____
Name: _____ Date: _____

FUNCTIONAL OUTCOMES OF SLEEP QUESTIONNAIRE (FOSQ)

Some people have difficulty performing everyday activities when they feel tired or sleepy. The purpose of this questionnaire is to find out if you generally have difficulty carrying out certain activities because you are too sleepy or tired. In this questionnaire, when the words "sleepy" or "tired" are used, it means the feeling that you can't keep your eyes open, your head is droopy, that you want to "nod off", or that you feel the urge to take a nap. These words do not refer to the tired or fatigued feeling you may have after you have exercised.

DIRECTIONS: Please put a ( ) in the box for your answer to each question. Select only one answer for each question. Please try to be as accurate as possible. All information will be kept confidential.

	(0) I don't do this activity for other reasons	(4) No difficulty	(3) Yes, a little difficulty	(2) Yes, moderate difficulty	(1) Yes, extreme difficulty
1. Do you have difficulty concentrating on the things you do because you are sleepy or tired?		☐	☐	☐	☐
2. Do you generally have difficulty remembering things, because you are sleepy or tired?		☐	☐	☐	☐
3. Do you have difficulty finishing a meal because you become sleepy or tired?		☐	☐	☐	☐
4. Do you have difficulty working on a hobby (for example, sewing, collecting, gardening) because you are sleepy or tired?	☐	☐	☐	☐	☐

Site: _____ ID #: _____
Date of Data Entry: _____ Trial _____
Name: _____ Date: _____

	(0) I don't do this activity for other reasons	(4) No difficulty	(3) Yes, a little difficulty	(2) Yes, moderate difficulty	(1) Yes, extreme difficulty
5. Do you have difficulty doing work around the house (for example, cleaning house, doing laundry, taking out the trash, repair work) because you are sleepy or tired?	❒	❒	❒	❒	❒
6. Do you have difficulty operating a motor vehicle for short distances (less than 100 miles) because you become sleepy or tired?	❒	❒	❒	❒	❒
7. Do you have difficulty operating a motor vehicle for long distances (greater than 100 miles) because you become sleepy or tired?	❒	❒	❒	❒	❒
8. Do you have difficulty getting things done because you are too sleepy or tired to drive or take public transportation?	❒	❒	❒	❒	❒
9. Do you have difficulty taking care of financial affairs and doing paperwork (for example, writing checks, paying bills, keeping financial records, filling out tax forms, etc.) because you are sleepy or tired?	❒	❒	❒	❒	❒

Site: _____ ID #: _____
Date of Data Entry: _____ Trial _____
Name: _____ Date: _____

	(0) I don't do this activity for other reasons	(4) No difficulty	(3) Yes, a little difficulty	(2) Yes, moderate difficulty	(1) Yes, extreme difficulty
10. Do you have difficulty performing employed or volunteer work because you are sleepy or tired?	☐	☐	☐	☐	☐
11. Do you have difficulty maintaining a telephone conversation, because you become sleepy or tired?	☐	☐	☐	☐	☐
12. Do you have difficulty visiting with your family or friends in <u>your</u> home because you become sleepy or tired?	☐	☐	☐	☐	☐
13. Do you have difficulty visiting with your family or friends in <u>their</u> home because you become sleepy or tired?	☐	☐	☐	☐	☐
14. Do you have difficulty doing things for your family or friends because you are too sleepy or tired?	☐	☐	☐	☐	☐

	(4) No	(3) Yes, a little	(2) Yes, moderately	(1) Yes, extremely	
15. Has your relationship with family, friends or work colleagues been affected because you are sleepy or tired?	☐	☐	☐	☐	

In what way has your relationship been affected? _____

_____

_____

Site: _____ ID #: _____
Date of Data Entry: _____ Trial _____
Name: _____ Date: _____

	(0) I don't do this activity for other reasons	(4) No difficulty	(3) Yes, a little difficulty	(2) Yes, moderate difficulty	(1) Yes, extreme difficulty
16. Do you have difficulty exercising or participating in a sporting activity because you are too sleepy or tired?	❒	❒	❒	❒	❒
17. Do you have difficulty watching a movie or videotape because you become sleepy or tired?	❒	❒	❒	❒	❒
18. Do you have difficulty enjoying the theater or a lecture because you become sleepy or tired?	❒	❒	❒	❒	❒
19. Do you have difficulty enjoying a concert because you become sleepy or tired?	❒	❒	❒	❒	❒
20. Do you have difficulty watching TV because you are sleepy or tired?	❒	❒	❒	❒	❒
21. Do you have difficulty participating in religious services, meetings or a group or club, because you are sleepy or tired?	❒	❒	❒	❒	❒

Site: _____ ID #: _____
Date of Data Entry: _____ Trial _____
Name: _____ Date: _____

	(0) I don't do this activity for other reasons	(4) No difficulty	(3) Yes, a little difficulty	(2) Yes, moderate difficulty	(1) Yes, extreme difficulty
22. Do you have difficulty being as active as you want to be in the <u>evening</u> because you are sleepy or tired?		❒	❒	❒	❒
23. Do you have difficulty being as active as you want to be in the <u>morning</u> because you are sleepy or tired?		❒	❒	❒	❒

	(0) I don't do this for other reasons	(4) No difficulty	(3) Yes, a little difficulty	(2) Yes, moderate difficulty	(1) Yes, extreme difficulty
24. Do you have difficulty being as active as you want to be in the <u>afternoon</u> because you are sleepy or tired?		❒	❒	❒	❒
25. Do you have difficulty keeping pace with others your own age because you are sleepy or tired?		❒	❒	❒	❒

	(1) Very Low	(2) Low	(3) Medium	(4) High
26. How would you rate your general level of activity?	❒	❒	❒	❒

Site: _____ ID #: _____
Date of Data Entry: _____ Trial _____
Name: _____ Date: _____

	(0) I don't engage in sexual activity for other reasons	(4) No	(3) Yes, a little	(2) Yes, moderately	(1) Yes, extremely
27. Has your intimate or sexual relationship been affected because you are sleepy or tired?	☐	☐	☐	☐	☐
28. Has your desire for intimacy or sex been affected because you are sleepy or tired?	☐	☐	☐	☐	☐
29. Has your ability to become sexually aroused been affected because you are sleepy or tired?	☐	☐	☐	☐	☐
30. Has your ability to "come" (have an orgasm) been affected because you are sleepy or tired?	☐	☐	☐	☐	☐

Thank you for completing this questionnaire.

APPENDIX E

SCORING INSTRUCTIONS FOR FUNCTIONAL OUTCOMES OF SLEEP QUESTIONNAIRE

FUNCTIONAL OUTCOMES OF SLEEP QUESTIONNAIRE (FOSQ)

Scoring Instructions September 1996 Version
(Revised 7/18/00)

Subscales	# Questions	Item #
General Productivity	8 questions	1 - 4, 8 - 11
Social Outcome	2 questions	12, 13
Activity Level	9 questions	5, 14 - 16, 22 - 26
Vigilance	7 questions	6, 7, 17 - 21
Intimate Relationships and Sexual Activity	4 questions	27 - 30

Subscale Scores: A response score of 0 for an item should be coded as a N/A or missing response. Thus, the potential range of scores for any item is 1 - 4. Calculate the mean of the answered items with responses equal to or greater than 1 for each subscale. This is the weighted mean item total or subscale score. For example, if a subscale has six questions, and one question has a missing response and one with a N/A response, then you would not include those two questions when you added the responses and you would divide by four instead of six when calculating the mean. This prevents a score bias due to missing answers or skipped questions because an individual does not engage in a particular activity do to reasons other than disorders of excessive sleepiness. The potential range of scores for each subscale is 1 - 4.

To obtain a Total Score: Take all of the subscale scores and calculate the mean of these scores and then multiply that mean by five. Multiply by five regardless of the number of subscales scores used in the computation of the mean. For example, if you a subscale score for all subscales, then you multiply the mean of those scores by 5; if you have subscale scores for only 4 of the 5 subscales, then you would also multiply the mean by five. The potential range of scores for the Total Score is 5 - 20.

APPENDIX F

PITTSBURGH SLEEP QUALITY INDEX

Pittsburgh Sleep Quality Index (PSQI)

For staff use only:
Global PSQI Score:_____

Instructions:

The following questions relate to your usual sleep habits during the past month only. Your answers should indicate the most accurate reply for the majority of days and nights in the past month. Please answer all questions.

1. During the past month, what time have you usually gone to bed at night?
   BED TIME_____
2. During the past month, how long (in minutes) has it usually taken you to fall asleep each night?
   NUMBER OF MINUTES_____
3. During the past month, what time have you usually gotten up in the morning?
   GETTING UP TIME_____
4. During the past month, how many hours of actual sleep did you get at night? (This may be different than the number of hours you spent in bed.)
   HOURS OF SLEEP PER NIGHT _____

For each of the remaining questions, check the one best response. Please answer all questions.

5. During the past month, how often have you had trouble sleeping because you...

	Not during the past month	Less than once a week	Once or twice a week	Three or more times a week
a. ...cannot get to sleep within 30 minutes	☐	☐	☐	☐
b. ...wake up in the middle of the night or early morning	☐	☐	☐	☐
c. ...have to get up to use the bathroom	☐	☐	☐	☐
d. ...cannot breathe comfortably	☐	☐	☐	☐
e. ...cough or snore loudly	☐	☐	☐	☐
f. ...feel too cold	☐	☐	☐	☐
g. ...feel too hot	☐	☐	☐	☐
h. ...have bad dreams	☐	☐	☐	☐
i. ...have pain	☐	☐	☐	☐
j. Other reason(s), please describe:				
How often during the past month have you had trouble sleeping because of this?	☐	☐	☐	☐

	Very good	Fairly good	Fairly bad	Very Bad
6. During the past month, how would you rate your sleep quality overall?	☐	☐	☐	☐

	Not during the past month	Less than once a week	Once or twice a week	Three or mor times a week
7. During the past month, how often have you taken medicine to help you sleep (prescribed or "over the counter")?	☐	☐	☐	☐
8. During the past month, how often have you had trouble staying awake while driving, eating meals or engaging in social activity?	☐	☐	☐	☐

	No problem at all	Only a very slight problem	Somewhat of a problem	A very big problem
9. During the past month, how much of a problem has it been for you to keep up enough enthusiasm to get things done?	☐	☐	☐	☐

	No bed partner or roommate	Partner/room mate in other room	Partner in same room, but not same bed	Partner in same bed
10. Do you have a bed partner or roommate?	☐	☐	☐	☐

If you have a room mate or bed partner, ask him/her how often in the past month you have had:

	Not during the past month	Less than once a week	Once or twice a week	Three or more times a week
a. Loud snoring	☐	☐	☐	☐
b. Long pauses between breaths while asleep	☐	☐	☐	☐
c. Legs twitching or jerking while you sleep	☐	☐	☐	☐
d. Episodes of disorientation or confusion during sleep	☐	☐	☐	☐
e. Other restlessness while you sleep	☐	☐	☐	☐

Please describe:_____

APPENDIX G

SCORING INSTRUCTIONS FOR PITTSBURGH SLEEP QUALITY INDEX

Pittsburgh Sleep Quality Index (PSQI)

Form Administration Instructions, References, and Scoring

Form Administration Instructions

The range of values for questions 5 through 10 are all 0 to 3.

Questions 1 through 9 are not allowed to be missing except as noted below. If these questions are missing then any scores calculated using missing questions are also missing. Thus it is important to make sure that all questions 1 through 9 have been answered.

In the event that a range is given for an answer (for example, '30 to 60' is written as the answer to Q2, minutes to fall asleep), split the difference and enter 45.

Reference

Buysse DJ, Reynolds CF, Monk TH, Berman SR, Kupfer DJ: The Pittsburgh Sleep Quality Index: A new instrument for psychiatric practice and research. *Psychiatry Research* 28:193-213, 1989.

Scores – reportable in publications

On May 20, 2005, on the instruction of Dr. Daniel J. Buysse, the scoring of the PSQI was changed to set the score for Q5J to 0 if either the comment or the value was missing. This may reduce the DISTB score by 1 point and the PSQI Total Score by 1 point.

PSQIDURAT

DURATION OF SLEEP
IF Q4 $\geq$ 7, THEN set value to 0
IF Q4 < 7 and $\geq$ 6, THEN set value to 1
IF Q4 < 6 and $\geq$ 5, THEN set value to 2
IF Q4 < 5, THEN set value to 3
Minimum Score = 0 (better); Maximum Score = 3 (worse)

PSQIDISTB

SLEEP DISTURBANCE
IF Q5b + Q5c + Q5d + Q5e + Q5f + Q5g + Q5h + Q5i + Q5j (IF Q5JCOM is null or Q5j is null, set the value of Q5j to 0) = 0, THEN set value to 0

IF Q5b + Q5c + Q5d + Q5e + Q5f + Q5g + Q5h + Q5i + Q5j (IF Q5JCOM is null or Q5j is null, set the value of Q5j to 0) $\geq$ 1 and $\leq$ 9, THEN set value to 1

IF Q5b + Q5c + Q5d + Q5e + Q5f + Q5g + Q5h + Q5i + Q5j (IF Q5JCOM is null or Q5j is null, set the value of Q5j to 0) > 9 and ≤ 18, THEN set value to 2

IF Q5b + Q5c + Q5d + Q5e + Q5f + Q5g + Q5h + Q5i + Q5j (IF Q5JCOM is null or Q5j is null, set the value of Q5j to 0) > 18, THEN set value to 3

Minimum Score = 0 (better); Maximum Score = 3 (worse)

PSQILATEN

SLEEP LATENCY
First, recode Q2 into Q2new thusly:
IF Q2 ≥ 0 and ≤ 15, THEN set value of Q2new to 0
IF Q2 > 15 and ≤ 30, THEN set value of Q2new to 1
IF Q2 > 30 and ≤ 60, THEN set value of Q2new to 2
IF Q2 > 60, THEN set value of Q2new to 3
Next
IF Q5a + Q2new = 0, THEN set value to 0
IF Q5a + Q2new ≥ 1 and ≤ 2, THEN set value to 1
IF Q5a + Q2new ≥ 3 and ≤ 4, THEN set value to 2
IF Q5a + Q2new ≥ 5 and ≤ 6, THEN set value to 3

Minimum Score = 0 (better); Maximum Score = 3 (worse)

PSQIDAYDYS

DAY DYSFUNCTION DUE TO SLEEPINESS
IF Q8 + Q9 = 0, THEN set value to 0
IF Q8 + Q9 ≥ 1 and ≤ 2, THEN set value to 1
IF Q8 + Q9 ≥ 3 and ≤ 4, THEN set value to 2
IF Q8 + Q9 ≥ 5 and ≤ 6, THEN set value to 3
Minimum Score = 0 (better); Maximum Score = 3 (worse)

PSQIHSE

SLEEP EFFICIENCY

Diffsec = Difference in seconds between day and time of day Q1 and day Q3

Diffhour = Absolute value of diffsec / 3600

newtib =IF diffhour > 24, then newtib = diffhour – 24

IF diffhour ≤ 24, THEN newtib = diffhour

(NOTE, THE ABOVE JUST CALCULATES THE HOURS BETWEEN GNT (Q1) AND GMT (Q3))

tmphse = (Q4 / newtib) * 100

IF tmphse ≥ 85, THEN set value to 0
IF tmphse < 85 and ≥ 75, THEN set value to 1
IF tmphse < 75 and ≥ 65, THEN set value to 2
IF tmphse < 65, THEN set value to 3
Minimum Score = 0 (better); Maximum Score = 3 (worse)

PSQISLPQUAL

OVERALL SLEEP QUALITY
Q6
Minimum Score = 0 (better); Maximum Score = 3 (worse)

PSQIMEDS **NEED MEDS TO SLEEP**
Q7
Minimum Score = 0 (better); Maximum Score = 3 (worse)

PSQI **TOTAL**

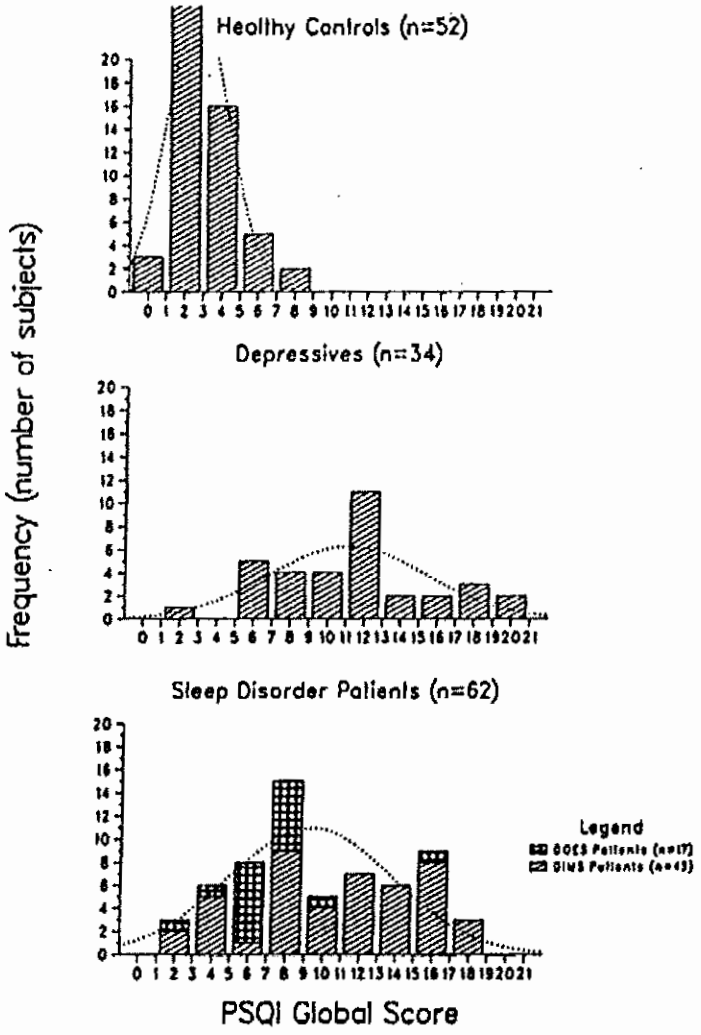
DURAT + DISTB + LATEN + DAYDYS + HSE + SLPQUAL + MEDS

Minimum Score = 0 (better); Maximum Score = 21 (worse)

Interpretation: TOTAL $\leq$ 5 associated with good sleep quality

TOTAL > 5 associated with poor sleep quality

Fig. 2. Pittsburgh Sleep Quality Index (PSQI) global scores



PSQI global scores showed different distributions for control subjects, depressed patients, and sleep-disorder patients. A global score cutoff of > 5 correctly identified 88.5% of all controls and patients, yielding a sensitivity of 89.6% and a specificity of 86.5% (Kappa = 0.75, $p < 0.001$).

Reference:
Buysse DJ, Reynolds CF, Monk TH, Berman SR, Kupfer DJ: The Pittsburgh Sleep Quality Index: A new instrument for psychiatric practice and research. Psychiatry Research 28:193-213, 1989.

APPENDIX H

PERCIEVED STRESS SCALE

For staff use only:
PSS Total Score: _____

Perceived Stress Scale

The questions in this scale ask you about your feelings and thoughts **during the last month**. In each case, you will be asked to indicate by circling *how often* you felt or thought a certain way.

0 = Never 1 = Almost Never 2 = Sometimes 3 = Fairly Often 4 = Very Often

1.	In the last month, how often have you been upset because of something that happened unexpectedly?	0	1	2	3	4
2.	In the last month, how often have you felt that you were unable to control the important things in your life?	0	1	2	3	4
3.	In the last month, how often have you felt nervous and "stressed"?	0	1	2	3	4
4.	In the last month, how often have you felt confident about your ability to handle your personal problems?	0	1	2	3	4
5.	In the last month, how often have you felt that things were going your way?	0	1	2	3	4
6.	In the last month, how often have you found that you could not cope with all the things that you had to do?	0	1	2	3	4
7.	In the last month, how often have you been able to control irritations in your life?	0	1	2	3	4
8.	In the last month, how often have you felt that you were on top of things?	0	1	2	3	4
9.	In the last month, how often have you been angered because of things that were outside of your control?	0	1	2	3	4
10.	In the last month, how often have you felt difficulties were piling up so high that you could not overcome them?	0	1	2	3	4

References:
Cohen, S., Kamarck, T., & Mermelstein, R. (1983). A global measure of psychological stress. *Journal of Health and Social Behavior*, 24, 385–396.

NPDS/OPC – PSS (Reviewed: Sep 2013)

APPENDIX I

SCORING INSTRUCTIONS FOR PERCEIVED STRESS SCALE

Perceived Stress Scale Score

The Perceived Stress Scale is a 10-item self report questionnaire that measures a persons' subjective appraisal of the stressfulness of the situations in the past 30 days.

- Each item is rated on a 5-point Likert scale ranging from *never* (0) to *almost always* (4).
- There are two subscales within the ten questions: 6 negatively worded questions and 4 positively worded questions. Question numbers 4, 5, 7, and 8 are the positively stated items. Questions 1, 2, 3, 6, 9 & 10 are the negatively stated items.
- Scores can range from 0 to 40, with higher scores indicating greater stress.

Score Calculation:

1. Reverse the scores on the four positive items (4, 5, 7 & 8): 0 = 4, 1 = 3, 2 = 2 and 1 = 1.
2. Negative item scores do not change (1, 2, 3, 6, 9 & 10): 0 = 0, 1 = 1, 2 = 2, 3 = 3 and 4 = 4
3. The overall PSS-10 score is the sum all 10 items.

Interpretation

The PSS is not a diagnostic instrument, so there are no cut-offs. There are only comparisons between people in a given sample. There are some normative data on the PSS based on a *1983 Harris Poll of a representative U.S. sample.

Higher PSS Scores are associated with:

- Higher levels of stress
- Increased stress interference with daily activity and quality of life
- Increased susceptibility to stress-induced illness
- Increased vulnerability to compromised health, especially if a significant life stressor (loss of a job, end of a relationship, death of a loved one, etc.) occurs in the near future

Question:	Score: (0-4)
1	
2	
3	
4 (reversed)	
5 (reversed)	
6	
7 (reversed)	
8 (reversed)	
9	
10	

Total Score: _____

*Total Score	*Your Perceived Stress Level is:	* Health Concern Level
6	Much Lower than Average	Very Low
7 - 10	Slightly Lower than Average	Low
11 - 18	Average	Average
19 - 22	Slightly Higher than Average	High
22 and over	Much Higher than Average	Very High

APPENDIX J

INSTRUCTIONS FOR TURNING TAP

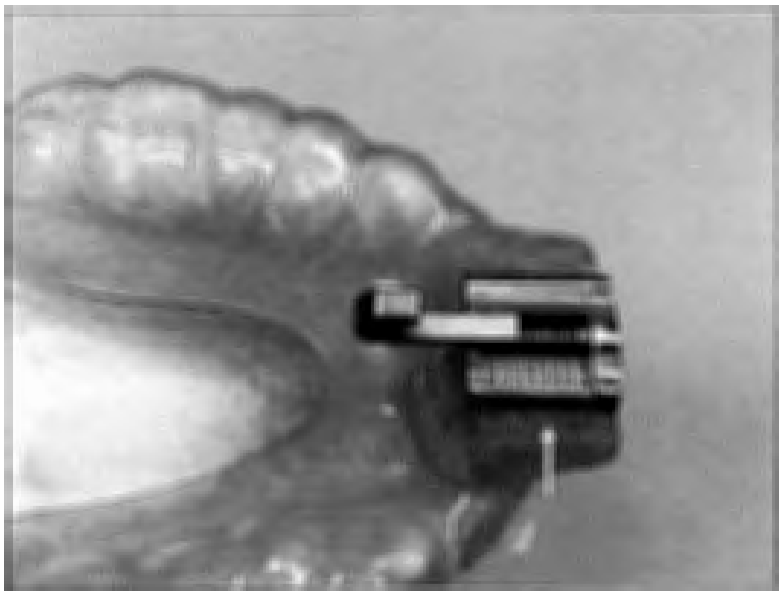


Fig 1: Device shown with hook set all the way back.

The second picture below shows the TAP advanced 2mm forward/ protrusive of the picture above. This was achieved by turning the key toward your left ear with the TAP in your mouth. Each half turn (i.e. 180°) brings the jaw forward 0.25mm. So to get from picture 1 to picture 2 in this example, the key was given 8 half turns. (8 x 0.25 = 2mm)

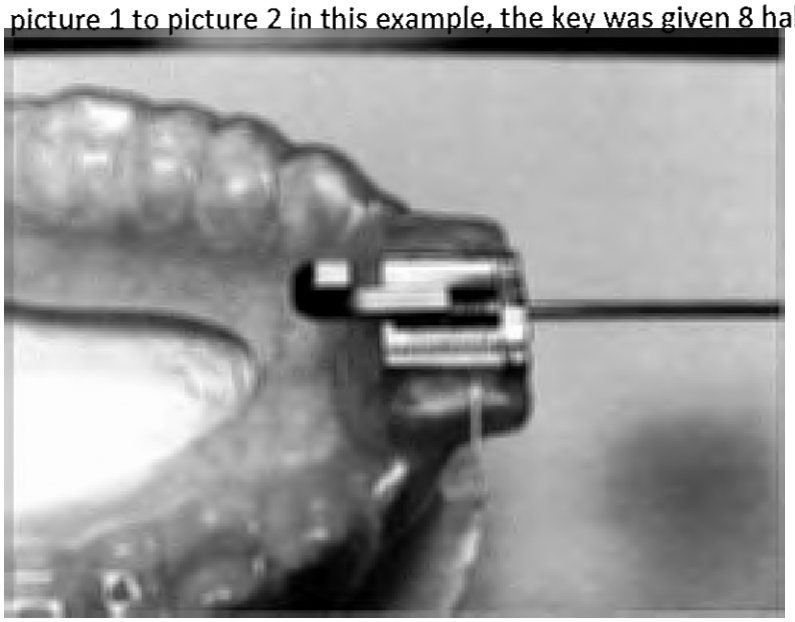


Fig 2: Device shown with hook advanced 2mm forward. Note position of the arrow pointing out the level at which the base of the hook is on the table. Here it is on the 4th mm line from the left. Compare to Fig 1 where the arrow is on the 2nd mm line from the left.

During the adjustment phase, advance the TAP by one half turn (180° = 0.25mm) every other night. This can be done with the key outside the mouth or in the mouth. If you get "lost", return the hook by dialing it back as far as it will go and it will look like Fig 1. ***Your <u>starting</u> point will be the _____ hash mark from the left.*** Do not advance the hook past the _____mm mark on the table (counting from the left) if applicable.
The TAP appliance was recorded at _____% of your maximum protrusive ability of _____mm.
The picture below shows the TAP in its most unprotruded position.

APPENDIX K

PERSONAL DATA LOG BOOK

Personal Data Log Book

Titration of Mandibular Advancement Device (MAD)

Visual Analogue Scales

INITIAL 7-DAY ACCLIMATION PERIOD LOG

DAILY TITRATION LOG

Study ID: _____

Sleep Study Daily VAS (Visual Analog Scales)

Study ID: _____ Date _____

Before Dinner: VAS for Day's Stress

Please rate how stressful your day was by making a mark on the 0 to 10 scale below. 0 represents a completely stress-free day and 10 represents the worst stress imaginable.

0 10

No Stress Worst Possible

Upon waking: VAS for Sleep Quality

Please rate the quality of each night's sleep by making a mark on the 0 to 10 scale below. 0 represents the worst sleep imaginable and 10 represents the best sleep imaginable.

0 10

Terrible Best Possible

Upon waking: VAS for any Jaw Pain

Please rate the amount of jaw pain you are experiencing upon awakening by making a mark on the 0 to 10 scale below. 0 represents no pain and 10 represents extreme pain.

0 10

No Pain Worst Possible

DO NOT FORGET TO FILL OUT THE DAILY TITRATION LOG

INITIAL 7-DAY ACCLIMATION PERIOD LOG

STUDY ID: _____

DATE (DD/MM/YY)	**RETIRE TIME** (HH:MM)	**RISE TIME** (HH:MM)	**APPLIANCE WORN?** (YES, NO)	**APPLIANCE WORN ALL NIGHT?** (YES, NO)	**ADJUSTMENT** 0=none +1= 1/2 turn clockwise (advance) -1=1/2 turn counterclockwise (reverse)	**PULSE OX WORN?** (YES, NO)	**Any Adverse effects** (If yes, Please describe on the notes page)	**Download Data & Charge battery (√)**
					0			X
					0			
					0			X
					0			
					0			X
					0			
					0			X

DAILY TITRATION LOG

STUDY ID: _____

DATE (DD/MM/YY)	**RETIRE TIME** (HH:MM)	**RISE TIME** (HH:MM)	**APPLIANCE WORN?** (YES, NO)	**APPLIANCE WORN ALL NIGHT?** (YES, NO)	**SCHEDULED ADJUSTMENT** (TOTAL ADVANCEMENT)	**SUBJECT ACTION** 0=none +1= 1/2 turn (180 deg) clockwise (advance) -1=1/2 turn (180 deg) counterclockwise (reverse)	**PULSE OX WORN?** (YES, NO)	**Any Adverse effects** (If yes, Please describe on the notes page)	**Download Data & Charge battery (√)**
					1/2 turn (0.25 mm)				X
					0				
					1/2 turn (0.5mm)				X
					0				
					1/2 turn (0.75 mm)				X
					0				
					1/2 turn (1.0 mm)				X
					0				
					1/2 turn (1.25 mm)				X
					0				

					1/2 turn (1.5 mm)				X
					0				
					1/2 turn (1.75 mm)				X
					0				
					1/2 turn (2.0 mm)				X
					0				
					1/2 turn (2.25 mm)				X
					0				
					1/2 turn (2.5 mm)				X
					0				
					1/2 turn (2.75 mm)				X
					0				
					1/2 turn=(3.0 mm)				X
					0				
					1/2 turn (3.25 mm)				X

					0				
					1/2 turn (3.5mm)				X
					0				
					1/3 turn (3.75 mm)				X
					0				
					1/2 turn (4.00 mm)				X
					0				
					1/2 turn (4.25 mm)				X
					0				
					1/2 turn (4.5 mm)				X
					0				
					1/2 turn (4.75 mm)				X
					0				
					1/2 turn (5.00 mm)				X
					0				

					1/2 turn (0.25 mm)				X
					0				
					1/2 turn (0.5mm)				X
					0				
					1/2 turn (0.75 mm)				X
					0				
					1/2 turn (1.0 mm)				X
					0				
					1/2 turn (1.25 mm)				X
					0				
					1/2 turn (1.5 mm)				X
					0				
					1/2 turn (1.75 mm)				X
					0				
					1/2 turn (2.0 mm)				X
					0				

					1/2 turn (2.25 mm)				X
					0				
					1/2 turn (2.5 mm)				X
					0				
					1/2 turn (2.75 mm)				X
					0				
					1/2 turn=(3.0 mm)				X
					0				
					1/2 turn (3.25 mm)				X
					0				
					1/2 turn (3.5mm)				X
					0				
					1/3 turn (3.75 mm)				X
					0				
					1/2 turn (4.00 mm)				X
					0				

					1/2 turn (4.25 mm)				X
					0				
					1/2 turn (4.5 mm)				X
					0				
					1/2 turn (4.75 mm)				X
					0				
					1/2 turn (5.00 mm)				X
					0				

NOTES & COMMENTS

Study ID No:

DATE (DD/MM/YYYY)	

APPENDIX L

SUBJECT DAILY LOG-60% PROTRUSION FOR 1 WEEK

SUBJECT # XX DAILY LOG - 60% protrusion for 1 week								
DATE (DD/MM/YY)	RETIRE TIME (HH:MM)	RISE TIME (HH:MM)	APPLIANCE WORN? (YES, NO)	ADJUSTMENT 0=none +1= 1/2 turn clockwise (advance) -1=1/2 turn counterclockwise (reverse)	PULSE OX WORN? (YES, NO)	ANY PROBLEMS?	FOLLOW UP APPOINTMENT	CHARGE BATTERY (1 hr)
				0				X
				0				
				0				X
				0				
				0				
				0				X
				0				
							X	

APPENDIX M

SUBJECT DAILY LOG-PAST 60%

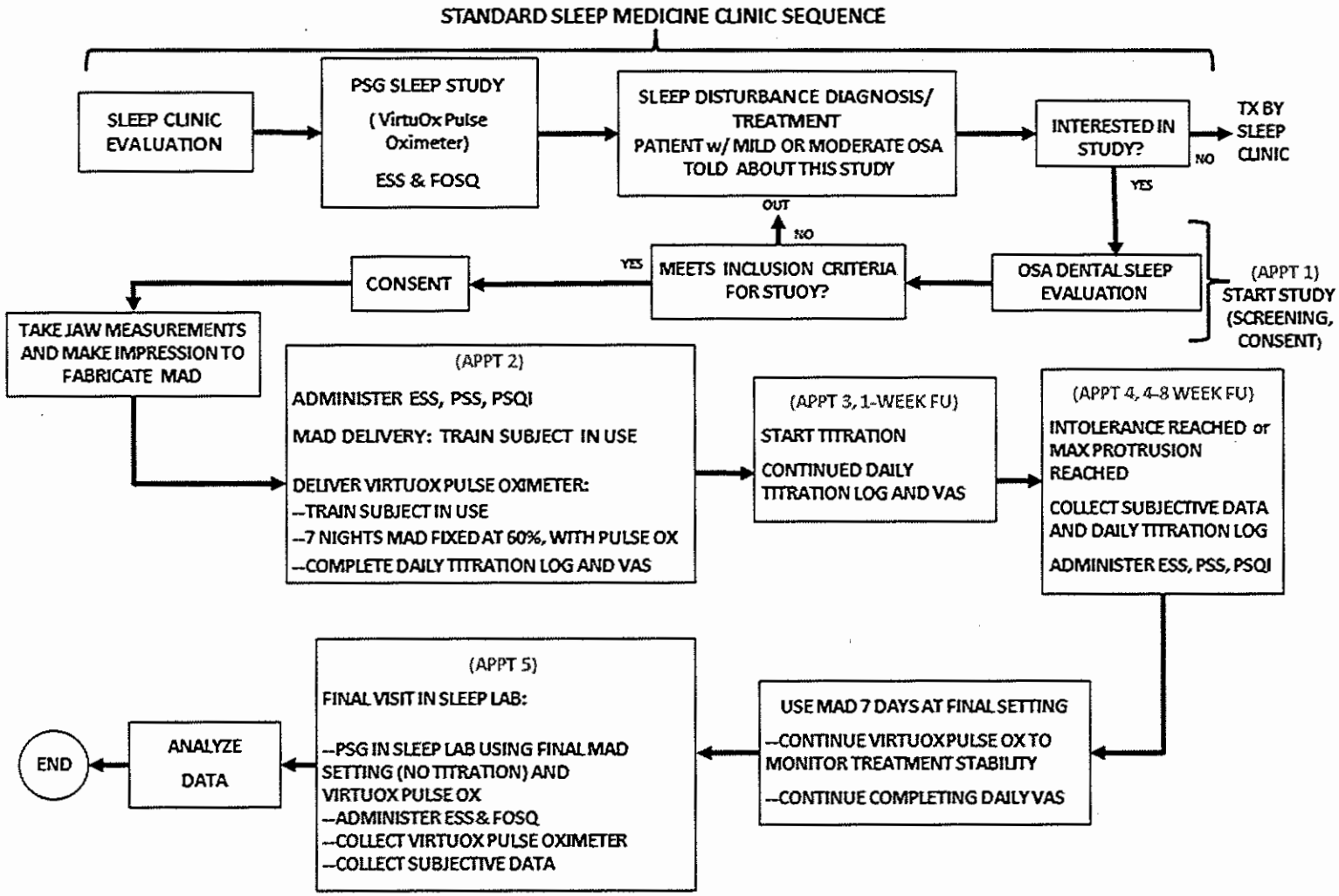
SUBJECT # XX DAILY LOG past 60%										
DATE (DD/MM/YY)	RETIRE TIME (HH.MM)	RISE TIME (HH.MM)	APPLIANCE WORN? (YES, NO)	APPLIANCE WORN? (YES, NO)	ADJUSTMENT (TOTAL ADVANCEMENT)	SUBJECT ACTION 0=none +1= 1/2 turn (180 deg) clockwise (advance) -1=1/2 turn (180 deg) counterclockwise (reverse)	PULSE OX WORN? (YES, NO)	ANY PROBLEMS?	FOLLOW UP APPOINTMENT	CHARGE BATTERY (1 hr)
					1/2 turn (0.25 mm)					X
					0					
					1/2 turn (0.5mm)					
					0					X
					1/2 turn (0.75 mm)					
					0					
					1/2 turn (1.0 mm)					X
					0					
					1/2 turn (1.25 mm)					
					0					X
					1/2 turn (1.5 mm)					
					0					
					1/2 turn (1.75 mm)					X
					0					
					1/2 turn (2.0 mm)					
					0					X
					1/2 turn (2.25 mm)					
					0					
					1/2 turn (2.5 mm)					X
					0					
					1/2 turn (2.75 mm)					
					0					X
					1/2 turn=(3.0 mm)					
					0					
					1/2 turn (3.25 mm)					X
					0					
					1/2 turn (3.5mm)					
					0					X
					1/3 turn (3.75 mm)					
					0					
					1/2 turn (4.00 mm)					X
					0					
					1/2 turn (4.25 mm)					
					0					X
					1/2 turn (4.5 mm)					
					0					
					1/2 turn (4.75 mm)					X

					0					
					1/2 turn (5.00 mm)					
					0				X Fit New Hook	X
					1/2 turn (0.25 mm)					
					0					
					1/2 turn (0.5mm)					X
					0					
					1/2 turn (0.75 mm)					
					0					X
					1/2 turn (1.0 mm)					
					0					
					1/2 turn (1.25 mm)					X
					0					
					1/2 turn (1.5 mm)					
					0					X
					1/2 turn (1.75 mm)					
					0					
					1/2 turn (2.0 mm)					X
					0					
					1/2 turn (2.25 mm)					
					0					X
					1/2 turn (2.5 mm)					
					0					
					1/2 turn (2.75 mm)					X
					0					
					1/2 turn=(3.0 mm)					
					0					X
					1/2 turn (3.25 mm)					
					0					
					1/2 turn (3.5mm)					X
					0					
					1/3 turn (3.75 mm)					
					0					X
					1/2 turn (4.00 mm)					
					0					
					1/2 turn (4.25 mm)					X
					0					
					1/2 turn (4.5 mm)					
					0					X
					1/2 turn (4.75 mm)					
					0					
					1/2 turn (5.00 mm)					X
					0				X	

APPENDIX N

STUDY FLOW CHART

Study Flow Chart



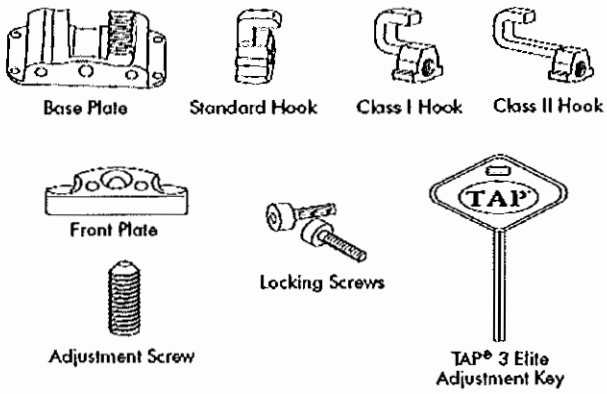
APPENDIX O

COLLECTED DATA SPREADSHEETS

Due to the large size of data spreadsheets, they can be found in electronic form on the Orofacial Pain departmental shared drive.

APPENDIX P

TAP 3-ELITE AND PROGAUGE



Permission to use Airway Management images smcclure@amisleep.com; www.tapintosleep.com

APPENDIX Q

VIRTUOX PULSE OXIMETER

VPOD transmits from patient's home

Data received via GPRS System

Oximetry Data received by VirtuOx Server

Report generates within seconds

Physician gets copy of result within minutes

Save Time And Money

Permission to use VirtuOx images kyle.miko@virtuox.net; www.virtuox.net

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